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THE INFLUENCE OF THE CYTOPLASM UPON GENE-CONTROLLED HEREDITY[1]

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GENETIC work of the last decades has almost completely centered around the study of the genes and their carriers, the chromosomes, of course for the reason that genetical methods have been specially devised for such studies. It has been silently accepted that the genes act on the cytoplasmic substratum of the cell in some way and control developmental processes, which are carried out by the gene and its products after all, not directly but *via* the protoplasm. No geneticist, of course, would doubt that the constitution of the cytoplasm is also specific in different forms. But most of them would not be ready to admit that the protoplasm might be the seat of definite hereditary properties in the same sense as this is true for the nucleus. The idea, occasionally pronounced by Boveri, again emphasized by Loeb and reappearing from time to time in other writings, that the characteristics of the tribe, family, and down to the species are laid down in the protoplasm and that only the varietal differences are controlled by the nucleus, has never found much favor with the geneticists; and the same is true for the less sweeping notion that there must be present in the protoplasm plasmatic genes of the type of nuclear genes. But of course the question of the protoplasm, not only as substratum for the action of the genes, but also as a part

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of the germ-plasm, directly influencing the hereditary traits by some action of its own, remains a problem which ought to be attacked by experimental methods.

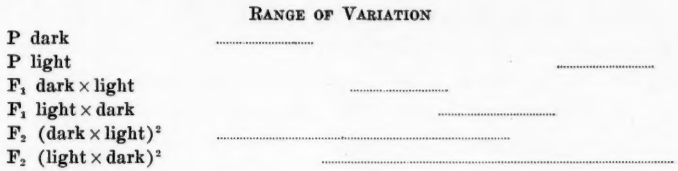
It is known that already in pre-Mendelian and in early Mendelian days experimental embryologists tried to attack this problem. There was, of course, Boveri's classic work on merogony which seemed to have solved it forever. Enucleated fragments of an Echinoderm species were fertilized with the sperm of a different species and larvae obtained with exclusively paternal characters, though regular hybrids proved to be intermediate. It is known that Godlewski had very different results in family-crosses with Echinoderms, where the larvae, as far as they developed, appeared to be purely maternal. There are some among us here who took part in the ensuing discussions. The climax was reached when Boveri, in a posthumous paper, had to state that there were sources of error in his former work and that reliably merogonic eggs died at early stages of development. Only recently, it seems, could this old problem be solved finally. Hörstadius was able to raise successfully hybrid merogonic larvae with Parechinus protoplasm and Echinus nucleus; they were intermediate in regard to skeleton characters and showed the influence of the maternal cytoplasm. A comparable experiment could be carried out by Harder in plants. In certain fungi (*Hymenomycetes*), a stage occurs after conjugation in which one of the cells contains a mixture of the protoplasm of both parents, but only one nucleus. This cell can be isolated and grown and if the two parents belonged to different forms, the influence of the mixed protoplasm as contrasted to the one nucleus could be studied. Certain hereditary traits showed only the influence of the nucleus, but others, especially the growth-habitus, appeared intermediate. That a comparable experiment, which Nawashin performed in *Crepis* by building up a plant with protoplasm of one and chromosomes of another species, had negative results as far as

protoplasmic influence was concerned, of course does not invalidate the positive results.

In these cases, the problem could be considered only in a more general way, that is, the effect of the whole nucleus within different cytoplasm was under discussion without a possibility of isolating the action of individual genes in different protoplasm. Now the genetic literature is overabundant with analyses of reciprocal crosses, in which the nuclei are alike in regard to individual genes, whereas the protoplasm is different according to the mother. In the overwhelming majority of cases in which the crosses are made between the wild form and its mutations or mutations *inter se,* no influence of the plasmatic constitution upon the result becomes visible. Reciprocal crosses and their offspring behave alike, of course with the exception of when genes within the X or Y chromosomes are involved, and other special purely chromosomal cases; we exclude of course from this statement also apparent cases of plasmatic action, which find a different explanation on closer inspection. I think, for example, of the cases of inheritance of plastid characters in plants, first studied by Correns. As plastids are usually not transmitted by the pollen tube, they must show a purely maternal inheritance. One might call the plastid a part of the protoplasm, but their bodily transmission is certainly not meant when we are discussing the cytoplasmic influence upon hereditary characters. But it seems that also border cases are existing in this field. Correns has described a case relating to a certain type of variegation where a condition of the protoplasm exists which prevents any plastids which enter it to form chlorophyll. Correns speaks of sick cytoplasm, thus expressing his view that he is not dealing with a case of ordinary cytoplasmic action. Another case of apparent plasmatic heredity, which turned out to be in fact chromosomal, is Toyama's much-quoted maternal inheritance. In these cases, first discovered for certain characters of the silkworm egg, reciprocal F_1-crosses behave completely ma-

ternally, F_2 shows normal dominance, as in typical F_1 generations, and F_3 shows Mendelian segregation as otherwise in F_2 with some special features. The explanation is, of course, that the characters in question are egg-characters, determined in the egg before fertilization; therefore, what is called the F_1-character is in fact the character of the mother and the actual F_2-generation is in fact, regarding these characters, only the F_1-cross. Similar cases have since been found, *e.g.*, the direction of coiling in snails, which is caused by a Mendelian gene influencing polarization of the egg-plasm (Diver-Boycott, Sturtevant, Crampton) or the strange case of hereditary gynandromorphism in the silkworm (Goldschmidt-Katsuki), where a Mendelian gene causes a definite abnormal behavior of the details of the reduction division before fertilization.

It is now very significant that though no cytoplasmic influence upon the action of genes in controlling visible characters has been found, when simple mutants were involved in the cross—one exception will be mentioned later—quite a number of cases with positive results are now available which have all in common that the systematic distance between the parents is considerably larger. If we omit at present the matroclinous species crosses which always have been suspected of being caused by cytoplasmic differences of the parents, the first properly analyzed case was found by myself 20 years ago. Some of you might remember an account of this work which I gave in a lecture at the Bussey Institution in 1915; but the evidence was only published in 1924 because I had always hoped to clear up one complication which pointed to the possibility of an additional influence of sperm-protoplasm. This point, however, finally had to be dropped. The Mendelian characters in question were differences between subspecies or geographic races of *Lymantria dispar,* namely, amounts of pigmentation in the caterpillars of different races. The type of heredity found we may indicate by the following diagram which practically applies to all other cases, too:



This means that F_1 is matroclinous and in F_2 a 1:2:1 segregation takes place, the range of which, however, is shifted in the reciprocal F_2 towards the maternal side. A corresponding effect was obtained also in back-crosses. The conclusion then was that it is not irrelevant for the action of the genes, on which or within which cytoplasm they are acting. Within the two races the respective phenotype was the result of the action of the genes, given the specific cytoplasm. If the same genes, however, were working within a different cytoplasm, the result of their action was shifted towards the type to which the cytoplasm belongs: Light genes in dark cytoplasm—to use these short designations—produce also in extracted homozygous condition a phenotype which is darker than the pure light race, and, *vice versa,* dark genes in light protoplasm fail to produce the completely dark forms among the homozygous segregants. If the same experiments were performed with different races distinguished by the presence of less and less light allelomorphs of the same dark gene, the same results were obtained but in a lesser degree. There can be no doubt that the geographic races in question were different in regard to some element of their plasmatic constitution. Since that time, other quantitative, germ-controlled characters in the same material were found to behave exactly in the same way—for example, length of hibernation and velocity of larval development.

In this piece of work, however, one important check was missing, namely, the analysis of the extracted homozygotes in further generations, which could not be made for technical reasons. But similar work has been done since with similar results and the additional filling of the

just-mentioned gap, at least in part. But we shall see soon that a decisive point is thus far not settled. There is, in the first line, Wettstein's work with mosses. This material permits crosses between races, species, genera and even subfamilies, whatever this might mean among bryologists. Generally speaking, the crosses between races of one species were reciprocally alike and did not show any influence of the cytoplasm upon the gene-controlled characters. All other combinations, however, showed such an influence, increasing with the taxonomic distance. Among the characters which were studied, some, like the form of the leaves, showed very clearly the plasmatic influence after the manner which we have just discussed for the Lymantria case, others showed it as less pronounced or not at all. In the case of the leaf-character it was possible in the species-cross to obtain a further back-cross generation which behaved according to the expectation, derived from the given explanation. In the generic cross no such direct way of testing was possible on account of the sterility. But it was to be expected that among those spores which are normally formed, because the respective gene-recombinations are viable, no difference of viability should exist between gene-recombinations of predominantly paternal or maternal origin. But as a matter of fact, more maternal recombinations were found in the reciprocal crosses, which is interpreted as meaning that the genes work more successfully with the cytoplasm of their own species. In this cross it was also possible to back-cross over again in succeeding generations with the paternal species, but the result was always maternal offspring, which shows that the supposed plasmatic incompatibility with the foreign chromosomes has not been changed. Unfortunately, also in this case the decisive experiment with extracted homozygotes in reciprocally different cytoplasm could not be performed, except for one generation of a back-cross on one side only, mentioned before.

One more case of a similar type in plants might be mentioned, because it shows again certain of the general features which we met thus far. Sirks found in his crosses with beans no reciprocal difference of crosses within the two sections of *Vicia faba* called major or minor. But in crosses between these sections, differences came to light which have to be regarded as of plasmatic nature. If a certain linkage group of genes is represented in a cross, the homozygous forms appear only in F_2 if the genes in question are situated in the protoplasm of the form from which they entered the cross. Otherwise they are not viable. In other words, the protoplasm of the major group is lethal for a certain chromosome derived in homozygous form from a minor plant. Or stated again another way: the chromosome in question contains either a lethal gene (or is as a whole lethal), which acts only in major-cytoplasm in a homozygous state.[2] In addition to this case, other cases were found which resemble our Lymantria case in that not only F_1 in reciprocal crosses is different, but also the segregants in F_2 are carried towards one direction by the cytoplasm. In our case, this direction was the direction towards the maternal type from which the cytoplasm sprang: light cytoplasm, for example, made all gene combinations lighter. In Sirks' case, however, the minor cytoplasm, for example, increased generally the action of certain growth-genes but decreased that of others, similarly with color-genes. This difference between the two cases can, however, not be considered as of primary importance. The subspecies of Lymantria, which were used, are distinctive natural forms, isolated from each other and therefore presumably well balanced in themselves through long selection. The subspecies of the beans, however, are cultural varieties and therefore probably not as distinctively balanced. It must be stated that, un-

[2] A case studied by Honing in Canna subspecies crosses is similar, but less extreme in plasmatic effect; others found by Skalinska and Gairdner fall in line.

fortunately, in Sirks' cases the analysis of further extracted generations is missing.

We mentioned before that all the cases of plasmatic difference, thus far known and recognizable by genetic methods, were found in crosses involving at least subspecies. This does not mean, however, that all such crosses must give this result. Baur, for example, reports that in his numerous crosses between geographic so-called species of *Antirrhinum,* no reciprocal differences were found. But as this material has not yet been worked up quantitatively, later work might change this statement. There has come to my attention, however, only a single case in which positive results have been found in an ordinary cross with mutations. Kuehn reported to have isolated by selection a strain of the wasp Habrobracon differing in intensity of body pigmentation from the stock. In crossing this form to the type, he reports results which practically repeat our results in Lymantria and are represented sufficiently by the diagram given above, with the exception of multiple genes being involved. This case is very remarkable because it is very difficult to imagine that through selection from a population simultaneously genic and corresponding plasmatic differences are selected. I must confess that I am expecting therefore another explanation for this unique case.

We have dwelt thus far mostly upon cases in which the conclusions regarding plasmatic influence upon the gene-controlled phenotype could be tested at least in the F_2 generation. But there is an additional set of facts derived from species crosses in plants, where no F_2-generation is available. Most of this work has been done in crosses between *Epilobium* species by Renner, Lehmann, Schwemmle and Michaelis. We shall try to isolate the decisive facts from the considerable body of details, facts which, however, are more nearly related to the experiments in merogony than to those discussed thus far, and still complicated by the fact that one of the char-

acters which has been studied, is pollen sterility. Crosses between different species may be reciprocally different. If they are different, always certain quantitative characters are involved, which appear to be inhibited in one cross. But there are also different biotypes found within one species which show this reciprocally different inhibition after crossing. If a hybrid is back-crossed to the paternal species and this is repeated over and over again in succeeding generations, finally plants are secured which contain practically only paternal chromatin within maternal cytoplasm. All their species characters resemble in fact those of the parental species, but the inhibitory action on quantitative characters, like corolla length and pollen fertility, remains constantly on the maternal side, as in F_1. No doubt then that a plasmatic influence upon gene-controlled characters is visible. We shall mention later some additional detail.

Let us try now to find out the general features of the facts just reported. The following conclusions seem to be warranted:

(1) There is a considerable number of cases known which show that the action of the genes in controlling hereditary traits is different, if the same genes are working within a different cytoplasmic substratum. In some cases this is known for definite genes, in others only for the whole genic outfit.

(2) The action of the cytoplasm might consist in shifting the genotype towards the type of the parent who has furnished the cytoplasm, that is, the mother. It might also consist in inhibiting the action of single genes or of all genes, if they are situated within a definite foreign cytoplasm; this inhibition might act only if the genes or whole chromosomes in question are present in the homozygous condition, but in other cases also in the heterozygous one.

(3) There are very few, if any, cases known in which this differential action of the cytoplasm is found in crossing different varieties or mutants of one species. But

the cytoplasmic difference appears rather frequently if subspecies and still more distant forms are crossed. As far as evidence goes, it seems that its effect upon the action of the genes increases with taxonomic distance.

(4) In one and the same case not all gene-controlled characters show the cytoplasmic influence. If we leave out of consideration general actions of inhibition and also complete incompatibility it seems that such characters are most liable to be affected by the cytoplasmic background, which are of a quantitative nature—size of organs or parts, amount of pigment, shapes of parts and similar characters.

The last-mentioned point now leads to the question whether we can derive any generalization regarding the cytoplasmic action under discussion. It seems that some botanists are inclined to assume that certain hereditary qualities may be transmitted by the cytoplasm in the same way as other characters are determined by the genes within the chromosomes. And the introduction of the term Plasmon by Wettstein for the entity of cytoplasmic action in heredity may be considered an outward sign of such a tendency. I can not help expressing my opinion that the facts do not encourage such a view. Where it was possible in the just-quoted cases to base the analysis upon individual gene-controlled traits, it was shown that no cytoplasmic heredity comes into play, but only a differential action of different plasmata as substratum upon the action of the genes in controlling the differentiation of definite characters. I do not think that a single case is known of a definite hereditary character which is determined as such by the hereditary constitution of the protoplasm, of course aside from the special case of plastid characters. I can conceive of the facts which have been reported only in one way: I assume that genes act in controlling the differentiation of hereditary traits through the control of chains of reaction of definite velocity. Whatever these reactions may be in individual cases, one thing may be regarded as certain: their veloci-

ties will be dependent among other things upon the substratum in which they take place, that is, the cytoplasm. The specificity of the cytoplasm in question may be physical, *e.g.*, a matter of viscosity, or it may be chemical like the pH situation, but in any case there is no reason to assume that it is of a type similar to the difference between two genes. It is then not a "plasmon," acting in some way as an independent part of the germ-plasm which is responsible for the phenomena in question, but simply some physical or chemical property of the cytoplasm of the species. And its most probable action is the inhibition or in other cases augmentation of velocities of gene-controlled developmental reactions, resulting in visible influences of cytoplasmic constitution upon such characters, which are influenced predominantly in their development by relative speeds of differentiation. In addition, of course, a kind of poisoning effect of wrong cytoplasmic surroundings might be involved in cases of sterility and the like.

Arrived at this point, we have to return to a fact which we mentioned repeatedly, namely, the incomplete knowledge of the behavior of the cytoplasmic influence in further generations of extracted homozygotes. The importance of this point for a final solution of the problem will become clear, if we turn now to the consideration of a possibility of interpretation, which has recently been tried rather successfully.

We have mentioned before that cases are known in which the genes obviously influence the behavior of the cytoplasm of the egg, *e.g.*, the case of the dextral and sinistral snails. We have to consider therefore at this point the question, whether after all the differences of cytoplasmic nature under discussion are not themselves the products of genic action. Of course such a simple relation is out of the question because this would result in a type of inheritance like Toyama's so-called maternal inheritance. But there is also another possibility. Jollos has discovered the strange phenomena of *Dauermodifi-*

kation: The action of external conditions changes certain characters of an organism and the change reappears in the next generation in a lesser degree and might continue thus for a number of generations until it finally disappears. There are a number of such cases in Protozoa and Metazoa known now, and it is quite obvious that the explanation which has been proposed is that the change in question is a cytoplasmic one, which only slowly, in the course of a few generations, is overcome by the action of the genes, controlling the normal cytoplasmic constitution. The experiments to test this interpretation agree thus far with it (Jollos), though it ought to be added that all decisive tests have not yet been performed. Jollos and Haemmerling have now pointed to the near relation of this body of facts to those reported before. If an experimentally induced *Dauermodifikation* may need up to 8 or 10 generations to disappear again, one might conclude that in the before mentioned experiments no proof is contained that the cytoplasmic difference between the two forms, which was originally present, remains so in spite of the presence of foreign genes. It might be quite possible that longer continued experiments would show that, just as in *Dauermodifikation* the effect of the stimulus disappears in the course of some generations, also the primary, natural plasmatic differences will slowly disappear under the influence of the genes of another form. This would mean that also the primary plasmatic differences of subspecies and species would be controlled by the genic constitution, but would be of such a nature that one series of ontogenetic processes under the control of different genes would not suffice to change it. As a matter of fact, there are some experiments available to test this problem. The method is to back-cross a hybrid which shows maternal influence over and over again with the father, so that the genes are finally mostly paternal, but the cytoplasm is still derived from the original mother. Wettstein performed this with the species crosses of mosses for a number of generations without finding a

change in the cytoplasmic influence. Michaelis, however, who performed the same experiment in *Epilobium,* found that all the characters which showed the cytoplasmic influence continued to do it after eight generations of paternal back-crossing, but with a clearly measurable reversion towards the paternal type. This of course is in favor of the views of Jollos, which we just represented. There can be no doubt that the decisive work in this field has still to be done.

We have mentioned thus far only cases in which ordinary somatic characters were involved. But there are some additional facts where the possibility of a cytoplasmic influence in sex-determination is under discussion, both in animals and plants. Correns studied a long time ago the behavior of gynodioecious plants like *Satureia* and *Cirsium,* in which pure females occur besides hermaphrodites. Hermaphrodites pollinated produce only hermaphrodites, and females pollinated with the pollen of hermaphrodites produce only females. The same result appears if the experiment is performed with different species of *Cirsium,* one of which is exclusively monoecious, the other gynodioecious. The result, namely, only female offspring, was not changed if in many succeeding generations the females were back-crossed over again to the hermaphroditic form. From these facts Wettstein derived the interpretation that the female plants contained something in their cytoplasm which inhibits the formation of the male organs. It might be said in favor of such a view that also in the species crosses of *Epilobium,* pollen fertility is decreased by cytoplasmic influence, and further that a comparable case of male sterility in flax, studied by Gairdner, and another in *Aquilegia* (Skalinska), found also its only probable explanation (given by Chittenden and Pellew) in the assumption of cytoplasmic inhibition of male differentiation.

Also in animals, the same problem reappears, namely, in Lymantria, but it is much more complicated. The

basic fact is that sex is determined by a quantitative relation between female and male determining factors. The male factors are genes situated within the X-chromosomes. The female factor, that is, the something which carries sex towards the female side, is inherited purely maternally as proven in the immense body of experiments on intersexuality. In ordinary crosses it could be shown that this maternally inherited female factor is not changed in ten and more generations, and the same is also true if long lines of complex crosses are made, introducing from the paternal side the chromosomes of many different sex-races over many generations, but leaving the maternal line untouched. The purely maternal inheritance of the factor controlling femaleness is therefore an experimental fact, which has stood more decisive tests than required. Whereas now in moths the female is the heterogametic sex, maternal inheritance may mean as well cytoplasmic inheritance as inheritance in the Y-chromosome. In my earlier papers I thought that the facts are in favor of the cytoplasm, but later some experiments were performed which swung the scale towards the Y-chromosome. If we cross a race with a very weak female factor with a male of a strong race, in F_1-females the weak female factor is combined with the strong male X-chromosome—to use this short expression—and this individual is, in spite of the female 1 X-constitution, transformed into a male. F_1 therefore consists of males only. Occasionally, however, about once in 300 individuals, a female appears which of course can be proven not to be due to an error. As daughter of a weak mother, she ought to contain also the weak female factor, which is inherited maternally. But in all the different tests for what is called weakness, these exceptional daughters behaved as strong females. There are only two explanations available: Either the cytoplasmic character, called relative strength of the female factor, whatever this may be, is able to mutate from weak to strong, just as a gene mutates; or the extra females

are the result of fertilization with a secondary non-disjunctional XY sperm cell, provided the female factor is situated within the Y-chromosome. Namely, an XXY male of the strong race possesses a strong Y from his non-disjunctional mother. If this male produces one Y-sperm in 150, this might fertilize an egg with X and produce an XY individual with a Y derived from the strong race to which the father belongs. If the female factor is situated within the Y-chromosome this would be a normal female, and in addition, a strong female. As indeed these extra-females behaved as strong females in all tests, I was inclined, with all caution, to assume that the maternal inheritance of the female factor is due to its situation within the Y-chromosome. During the last years I have now prepared a crucial experiment, which has been finished successfully only a couple of weeks ago. Without going into the genetical details, it was performed the following way: We just mentioned the all-male broods obtained by crossing weak females to strong males. These F_1-males of course consist of one half genuine males with XX and one half genetic females transformed into XY-males. If the Y of these contains the female factor, it must be a weak one, as it is derived from the weak mother. Now the genuine males and the males by transformation can not be distinguished externally. To test them, therefore, we must mate every single male of a brotherhood. This mating is done with neutral or strong females, that is, females containing a female factor of such strength that never female intersexuality or transformation of females into males can occur in their offspring or further on in the maternal line. Now we come to the decisive point. If these females are mated to normal males, the offspring is normal and the daughters behave of course like ordinary strong females. But what will be the consequence, if the strong female is mated to a male by transformation possessing an X and a weak Y? Among the offspring of this male will be ordinary females, receiving their X from the

father and their Y from the mother. And whereas this is a strong Y, they must behave in future crosses like ordinary strong females, whether the female factor is situated within the cytoplasm or the Y-chromosome. But the male by transformation produces also Y-sperm, which will determine daughters, if fertilizing an egg with X. These daughters now are in possession of a weak Y, derived from the weak paternal grandmother. If the female factor is situated within the Y-chromosome, then these daughters must behave like weak females, that is, must produce only sons if mated now to a strong male. If, however, the female factor is inherited within the cytoplasm, also these females will behave as strong ones, give normal offspring with strong males. This experiment has now been performed on a large scale, involving altogether 40,000 to 50,000 individuals. From the sex ratio in the second generation it could be ascertained that actually the XY-males by transformation of the first generation had procreated offspring. About 400 daughters of both types of males, normal and by transformation, were tested by breeding to strong males. In every single case the offspring contained both sexes. This experiment definitely rules out the Y-chromosome as the seat of the female factor in Lymantria, which turns out to be a property of the cytoplasm. It is very significant that the different grades of strength of the female factor which are found in a definite order in the different geographic races of Lymantria are based on cytoplasmic properties, which run to a certain extent parallel to other cytoplasmic actions found in the same races. The same problems, then, which were raised for other cases of plasmatic differences apply also to this case. The most important of these is the relation between the genes and the cytoplasm as far as a control of cytoplasmic constitution by definite genes is involved, a problem which we met before while discussing the questions relating to *Dauermodifikation*. As a matter of fact, we know quite a number of autosomal genes in Lymantria which act as modifiers on the

expression of femaleness. There is no doubt, then, that the quantitative amount of influence of the cytoplasmic female action can be controlled by autosomal genes. But the basic cytoplasmic differences which we mean when speaking of the different grades of strength of the female factor have thus far been found to be uninfluenced by genes over a considerable series of generations. But I do not intend to go into further details, which belong more to the sphere of the problem of sex-determination.

Summarizing the contents of this paper we might say that distinctive cytoplasmic influence upon the action of genes in controlling hereditary traits has been found in many instances, an influence which seems to increase with taxonomic difference. It has not yet been decided whether this influence is purely cytoplasmic or under control of genes in the form of *Dauermodifikation.* A special rôle is assigned to the plasmatic influence in sex-determination. May I finish by saying that the problems of which we made a short survey would deserve further experimental attack, which might lead to far-reaching conclusions.

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PHYSIOLOGICAL AND EVOLUTIONARY THEORIES OF DOMINANCE[1]

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INTRODUCTION

MENDEL found that one member of each of his seven pairs of alternative characters of the pea reappeared in the first cross-bred generation to the complete or nearly complete exclusion of the other. Although he attributed no great importance to this himself, there was some tendency, following the rediscovery in 1900, to consider a law of dominance as one of the fundamental principles of heredity. It has long fallen from this estate and it has been questioned whether careful measurements would not show complete dominance to be the exception rather than the rule. An approach to complete dominance is common enough, however, to present a number of interesting problems.

In the first place, it is clear that dominance has to do with the physiology of the organism and has nothing to do with the mechanism of transmission, *i.e.*, with heredity in the narrow sense. Studies of dominance bear on two different groups of problems. The accurate measurement of degree of dominance of particular genes under varying conditions furnishes one of the most available tools for carrying physiological analysis back to the ultimate controlling factors. On the other hand, statistical generalizations in regard to dominance may rest not only on the average consequences of physiological principles but also on general evolutionary trends and thus may throw light on the evolutionary process.

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PART I. STATISTICAL PRINCIPLES OF DOMINANCE

Generalizations

Among the statistical generalizations which have been made are the following: (1) Dominance of one allelomorph is the rule. (2) The recessive genes are usually less advantageous to the species than their dominant allelomorphs. (3) The effect of the recessive is usually the absence of a positive property found in the dominant in those cases in which there seems to be an approach to knowledge of the primary gene effects. (4) The recessive genes are usually less abundant in natural population than their dominant allelomorphs. (5) In cases in which origin is known the mutant gene is usually recessive. All of these principles are subject to much qualification.

Conditions in Natural Populations

With regard to the last two, we must carefully distinguish between the properties of uncommon genes found in natural population and those of observed mutations. The evolutionary problems are somewhat different. Even if mutation of all sorts, dominant, semi-dominant and recessive, occurred at random, these properties would not remain distributed at random in a population. Most mutations are observed to be injurious as is to be expected if a mutation is of the nature of an accident to a gene. Injurious dominant and semi-dominant mutations are vigorously selected against and kept at low frequencies ($q = \frac{u}{hs}$ where u is rate of recurrence of the particular mutation and s is the selective disadvantage per generation of the homozygous mutant, hs that of the heterozygote). A mutation that happens to be completely recessive is largely protected from selection and will be kept at relatively high frequencies in the population ($q = \sqrt{u/s}$). With one per cent. selective dis-

crimination against homozygous mutants ($s = .01$) and a rate of recurrence of one in a million per generation, deleterious recessive genes will be kept at 50 times the frequency of ones with exactly intermediate heterozygotes and 100 times that of equally deleterious dominants. Thus the first four of the above principles as applied to genes in natural populations are readily understandable (assuming that most mutations interfere with, rather than increase, the development of characters), without assuming any special tendency for mutation to be recessive.

There is, however, abundant evidence that this is not the whole story. Observed mutations in general are not only injurious and manifested generally in loss of characters, but are actually much more frequently recessive than dominant or semi-dominant.

THE PRESENCE AND ABSENCE HYPOTHESIS

The first widely accepted hypothesis was Bateson and Punnett's theory of presence and absence. They assumed that the commonest type of mutation was simply loss of a positive entity, that loss of a gene brought loss of the corresponding character (3) that such loss was usually injurious (2), and usually recessive (5) on the principle that the presence of one dose of a positive entity should give results more like those of two doses than like none at all (a law of diminishing returns). The observed phenomena of dominance were thus accounted for on the basis of a physiological theory of the relative effects of presence and absence and a theory of the prevailing nature of mutation.

I need not dwell long on the difficulties with this theory that have rendered it unacceptable. Among these have been the discovery of numerous series of multiple allelomorphs, not always to be interpreted as quantitative series, the observation of dominant effects from known losses of genes (*e.g.*, Haplo IV. and Notch in Drosophila) and particularly the demonstration of reverse mutation

from recessive mutant genes. There is also the difficulty of accounting for evolution, if mutation is wholly a matter of loss, to which Bateson himself drew attention.

Selection of Modified Heterozygotes

R. A. Fisher (1928a, b, 1928, 1930, 1931) has attempted to account for the prevailing dominance of wild type over rare and deleterious mutations as the result of a long continued process of selection of heterozygotes toward resemblance to wild type. With respect to the necessary physiological basis, he merely assumes that intermediacy of the heterozygote is the most natural condition.

The physiological basis of dominance on this view is the assemblage of a very special group of modifying factors under pressure of natural selection. He assumes, doubtless correctly, that the mutations observed in the laboratory must have recurred innumerable times in the history of the species. He notes that heterozygotes, while uncommon, must always have been enormously more common than homozygous mutants and concludes that the selective advantage of those heterozygotes which most closely resemble wild type would result in the end in carrying them to identity of appearance (and physiology) with wild type.

I have criticized this theory on the ground that the selection pressure would be too small to be the controlling factor in the fixation of the postulated modifiers of dominance (1929a, b). I will take this opportunity to correct a slight error in the formulae.

Let A, a be the type and mutant genes respectively.
Let M be a modifier which causes Aa to approach AA, but which has no effect on AA.

It is convenient to assume dominance of M as the most favorable case.

Let q_M be the frequency of M, $(1-q_M)$ that of m.
Let s be the selective disadvantage of aa (compared with AA).
Let hs be the selective disadvantage of Aamm (compared with AA).
Let h's be the selective disadvantage of AaM– (compared with AA).
Let h"s be the net selective disadvantage of Aa (compared with AA).

$$h'' = (1 - q_M)^2 h + [2q_M (1 - q_M) + q_M^2] h'.$$

Let u be rate of mutation from A to a per generation.

The opposed pressures of mutation and selection would keep the frequency of gene a at the point $\frac{u}{h''s}$. The genotypes would be distributed according to the expansion of the following expression.

$$\left[\frac{u}{h''s} a + \left(1 - \frac{u}{h''s}\right) A\right]^2 \left[(1 - q_M)m + q_M M\right]^2.$$

The selective disadvantage of the mm individuals as a group (compared with AA) is $2\frac{u}{h''s}\left(1 - \frac{u}{h''s}\right)hs + \left(\frac{u}{h''s}\right)^2 s$, or $\frac{2uh}{h''}$ ignoring second order terms. Similarly that of M— individuals is $\frac{2uh'}{h''}$ to a sufficient approximation. The advantage of M— over mm may be written $s_M = \frac{2u(h - h')}{h''}$.

The most favorable case is that in which the modifier is not only dominant but also produces complete dominance of A over a at a single step. In this case $h' = 0$, $h'' = (1 - q_M)^2 h$ and $s_M = \frac{2u}{(1 - q_M)^2}$.

The rate of change per generation of frequency of the dominant gene M is of the form

$$\Delta q_M = s_M \; q_M \; (1 - q_M)^2. \qquad \text{(Wright, 1931)}$$

Substituting,

$$\Delta q_M = 2u q_M. \qquad (1)$$

If gene M were mutating to m at a rate only twice that at which A it mutating to a, its frequency would change at the rate $\Delta q_M = -2u q_M$, exactly neutralizing the above selection pressure.

But this selection pressure is the maximum possible under Fisher's hypothesis (in the case of rare mutation).

In general, single modifiers of dominance could not be expected to produce complete dominance by themselves nor would they always be completely dominant. Thus in general, selection favoring the heterozygotes of rare mutations would tend to change the gene frequencies of modifiers much more slowly than would recurrent mutation at ordinary rates.

There is no disagreement over the magnitude of the effect of selection here. Fisher's contention is that the action of a steady selection pressure, however minute, would be effective if continued long enough. Yet he states elsewhere of mutation pressure "for mutations to dominate the trend of evolution, it is thus necessary to postulate mutation rates immensely greater than those which are known to occur." I quite agree with this statement and it has accordingly seemed to me that still smaller selection pressures would be practically negligible in determining which phase of the modifier approached fixation. There should always be other evolutionary pressures of greater magnitude acting in one direction or the other.

In particular, if the modifier has any effect on its own account which is subject to selection (*i.e.*, if the combination AAM — has any advantage or disadvantage relative to AAmm the pressure due to such selection is certain to take precedence over that due to its effect on the rare heterozygote. Haldane (1930a) has made essentially the same criticism. His form of statement brought out the likelihood that a modifier of the heterozygote would be for a similar reason a modifier of the much more abundant wild type, while I emphasized more the point that even in those cases in which the homozygote is not capable of being modified in the same respect as the heterozygote, the modifier is likely to have other effects subject to direct selection.

If this hypothesis is untenable what alternative is there? I believe that little progress can be made without development of a physiological theory. It must be re-

membered that whatever the evolutionary mechanism by which a particular gene complex has been reached, the state of dominance of all of the genes in the complex must always have a completely physiological explanation.

PART II. PHYSIOLOGICAL EXPLANATIONS OF DOMINANCE

THE FACTORS OF DEVELOPMENT

The development of such a theory is of course a rather speculative matter. It involves the whole question of the mechanism of control of the developmental process. However, the present states of knowledge of embryology and physiology impose certain limitations on speculation. We are sure, for example, that development is an epigenetic process. The genes can not stand in the simple one to one relation to morphological characters of a preformationist theory. Genetic data are of course in harmony. Each character is affected by many genes and each gene affects many characters.

Any particular physiological process occurring at a particular time and place in the history of the organism is the resultant of a complex of factors (Fig. 1). These may conveniently be grouped in four categories.

First, is the chain of past events in the same region. These give in general a continually narrowing field of potentialities associated with an increasing capacity for self differentiation, as development proceeds.

Second, is the array of correlative influences emanating from other regions, by means of which the region in question comes to fill a place in the integrated pattern of the organism as a whole. Among these are relations of physiological dominance in the sense of Child, embryonic inductions, mechanical stresses, hormone effects, stimulation through the nervous system and perhaps mitogenetic rays.

The internal environment, thus constituted, must be sharply distinguished from a third class of factors, the

direct influences from the external world. Little importance can be attributed to these in controlling the course of normal embryonic development, apart from the establishment of a primary simple gradient pattern by trivial differential stimuli, the maintenance of differential conditions at the surface, and of course the supply of the necessary conditions for life.

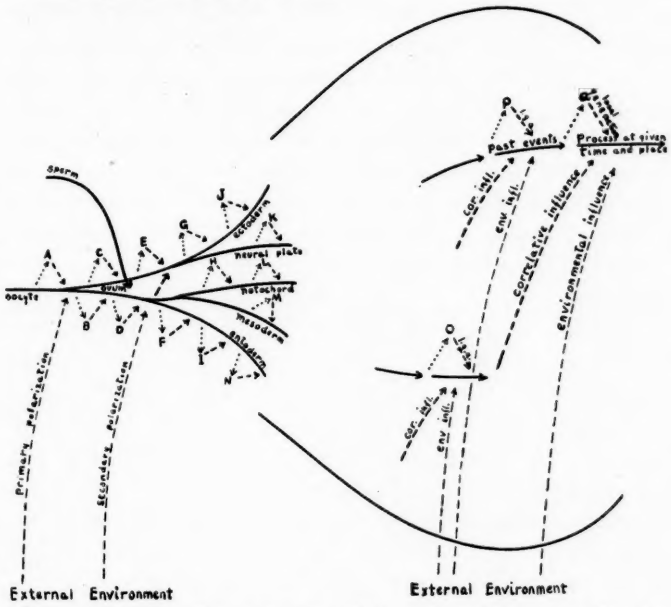

FIG. 1. Diagram illustrating the relation of factors to any developmental process of a vertebrate, occurring at a particular time and place. The letters A to Q represent genes which affect the process in question.

Finally an event in the place in question may be the result of current activity of genes in its own cells.

These are obviously not final terms, except in the case of external influences. On following the history of our region a step back, analysis can again be made in terms of these four classes of factors. Similarly each correlative influence traces to events in other parts of the body which are capable of the same sort of analysis. Ulti-

mately all chains begin either in an external stimulus somewhere or a gene action somewhere. But gene action is not a final term. The gene is presumably called into play at a particular time and place by conditions external to it. These conditions may simply be ones that present it with its proper substrate for action, but it is possible that in some cases there is activation of a mutational nature.

It has been usual for geneticists to assume that all cells of an organism contain the same array of genes, as a necessary consequence of the equational character of mitosis, and that differentiation depends merely on differential responses of this uniform heredity to diverse local environments. But genes which mutate so frequently as to bring about genetic differentiation of the tissues of every individual in a strain were long ago discovered by Correns in variegated plants. Emerson and his coworkers have shown that mutation in variegated corn is not merely a result of chance. Demerec (1929) has shown that a similar type of mutation in *Drosophila virilis* is brought to some extent under control of local conditions (stable in gonads, highly mutable in wings) in the presence of specific genes. The resulting situation closely resembles that of the familiar spotting patterns of mammals ranging from the highly irregular piebald of guinea-pigs to the orderly one of hooded rats. At present, the most plausible explanation of these is that they depend on genes which mutate in relation to a more or less regular gradient pattern in the embryonic skins, although proof of the type given by Demerec is lacking because of the stability of the genes in the germ plasm (*e.g.,* through 30 generations of brother-sister mating in guinea-pigs). There is here a suggestion that diphasic genes, stable in the germ plasm, but regularly and irreversibly changing phase in parts of the soma in response to specific stimuli, may be of general importance in stabilizing otherwise labile embryonic patterns.

In any event, on continuing to trace back, the various paths should ultimately be found to be diverging from a relatively small number of gene activities in the egg and, even earlier, in the oocyte. Through such mechanisms, a primary merely quantitative pattern of metabolic activity, due to external relations (Child), may be elaborated along branching paths, possibly involving irreversible nuclear changes (perhaps related to the embryonic segregation of F. R. Lillie) to any degree of complexity as a largely self-contained system.

The Chain of Reactions between Gene and Character

If we isolate from this network a chain of processes connecting a single gene action with an observed character, we reach a representation of the type of Fig. 2.

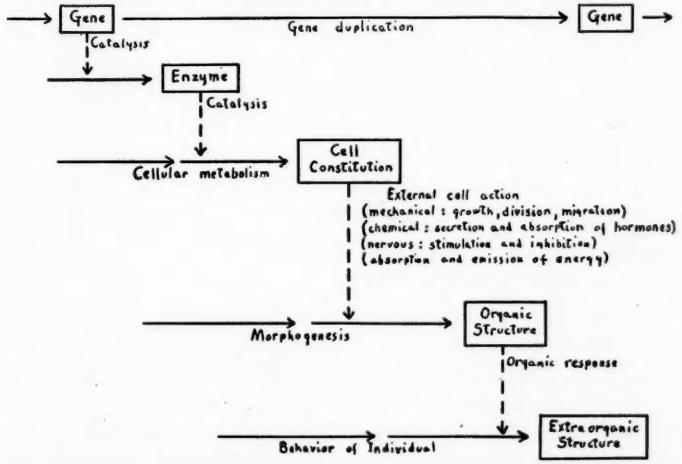

Fig. 2. Diagram illustrating the chain of processes relating the immediate physiological action of a gene to characters at different levels.

Since the genes are contained within the nuclei of cells, it is obvious that a genetic difference in any character must trace back to a difference in a cell character—rate of growth and division, orientation of mitotic spindle,

movement in response to stimuli, production of specific substances, etc. In some cases the chain of developmental processes between gene and character may be fairly short. Danforth (1928, 1929), for example, has shown by transplantation experiments that the differences between breeds of poultry in color, in rate of growth of feathers (as affected by the well-known sex-linked genes, but not by another factor) and in the form of feathers of males of hen-feathered and cock-feathered breeds all depend on gene differences in the cells of the feather follicles themselves. The study of gynandromorphs and other mosaics in *Drosophila* reveals that with a few interesting exceptions the observed character differences depend on local gene action. The same is shown by somatic mutations to be true of most at least of the color variations of guinea-pigs (Wright and Eaton, 1926). On the other hand, numerous experiments show that the difference between male and female fowls in color and form of feathers do not depend on local genes but on genetic differences elsewhere, *i.e.*, the presence or absence of an ovarian hormone, probably tracing in normal birds to differential gene action in the cells of the embryonic gonad, although the chain may be still longer. Similarly, Smith and MacDowell (1930) have demonstrated that a type of dwarfism, shown by Snell (1929) to be a simple recessive, depends on a deficiency of the anterior pituitary. The gene difference between these mice and normals exists in all cells of the body, but differential action apparently occurs only in the pituitary. The chains of reactions may be even longer. The characteristic specific, generic and familial differences between the webs of spiders are as clearly hereditary as are the differences in arrangements of their eyes, but must trace to their genetic basis through somewhat longer chains of processes. It is important to recognize that there is no essential difference in the relation of character to gene in these cases. The form of the web is a resultant of the behavior of the organism as a whole, the arrangement of

the eyes is a resultant of cellular behavior. The ultimate differential factor between species in both cases presumably resides in the nuclei of cells called into action somewhere in the organism.

As to the chains of intracellular processes, physiologists seem agreed that the specific syntheses to which differences in constitution and behavior of cells trace, depend on the presence of specific catalysts—enzymes. Cuénot, as early as 1903, suggested that the color genes of the mouse act in part through control of the production of specific enzymes. Since then the suggestion has been made repeatedly by both geneticists and physiologists that this is the characteristic mode of action of genes.

Enzyme differences have been demonstrated to be associated with gene differences in a considerable number of cases. One of the most interesting is Brink's demonstration of a reduction in amylase content in pollen grains containing the recessive gene wx of waxy corn as compared with those containing its normal allelomorph. Only slightly less direct, however, is the relation established between genetic constitution and the presence or absence of oxidases and of oxidase inhibitors in the skin of mammals (Onslow, Schultz, Kröning, Koller and others). In other cases it has been established by tracing the embryonic history, that a genetic character difference is first manifested as a difference in rate of reaction, strongly suggestive of enzyme control. Goldschmidt (1927) has presented a number of beautiful examples in Lepidoptera. Of especial importance is his evidence that differences which on first analysis depend on regulation of time of onset or cessation of a reaction, on further analysis can be shown to depend on rates. Ford and Huxley (1927) have given an analysis of variation in eye color of Gammarus in similar terms.

The genes themselves would seem to belong to the class of catalysts from mere consideration of the definitions of the two terms (Goldschmidt, 1916, Troland,

1917). Whatever reactions genes may bring about, it appears that they remain constant in the amount per cell, through duplication (autocatalysis) and separation in orderly relation to cell division. Brink's case is of interest here as one in which the same gene clearly produces physiological effects in the pollen grain without being destroyed thereby.

It is hardly likely, however, that the genes are themselves the enzymes immediately responsible for observed cell products: that Brink's extracted amylase or Onslow's tyrosinase, for example, actually consist of genes. The fact that the genes are in the nucleus while specific cell products (such as starch grains and pigment granules) are elaborated in the cytoplasm suggests that genes, as catalysts, act largely through control of the production of other catalysts, the extractible enzymes.

With the character in general at many additional removes from the primary gene action, it is obvious that no single theory can be expected to account for all cases of dominance.

As regards the mere question of frequency of dominance, however, it is obvious that a condition at any link in the long chain between gene and character, which causes identity of expression in the heterozygote and one of the homozygotes will thereby result in dominance at all later links. The chance of intermediacy persisting to the final character is thus only that for a typical link raised to a power as great as the number of links in the chain.

MATHEMATICAL THEORY

As a starting point, let us consider the conditions for dominance at a single link in such a chain and since rate effects seem to be more fundamental than timing or duration effects, let us consider the relation between amounts of catalyst and the amount of product in a chain of practically irreversible transformations during a period in which the amounts of intermediary substances may be treated as in flux equilibrium. The transformations will

be assumed to be such that they can be treated as monomolecular, and the rate of reaction will be assumed to depend jointly on the concentration of the substrate and of the catalyst.

Assume that the substance Y (Fig. 3) is supplied at a

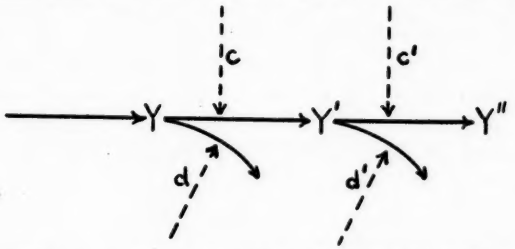

FIG. 3. A chain of monomolecular transformations.

constant rate C, that it is transformed into Y′ at a rate per unit mass c and that it is otherwise disposed of at a rate per unit mass d. The product Y′ is disposed of constructively (forming Y″) and destructively at the respective rates per unit mass c′ and d′. Y″ is treated as a final product. The rate of change of each substance (except Y″) is to be equated to zero, to represent the postulated state of flux equilibrium.

$$\begin{aligned} \frac{dY}{dt} &= C - (c+d)\,Y = 0 & Y &= C\left(\frac{1}{c+d}\right) \\ \frac{dY'}{dt} &= cY - (c'+d')\,Y' = 0 & Y' &= C\left(\frac{c}{c+d}\right)\left(\frac{1}{c'+d'}\right) \\ \frac{dY''}{dt} &= c'Y' & Y'' &= C\left(\frac{c}{c+d}\right)\left(\frac{c'}{c'+d'}\right) \end{aligned} \qquad (2)$$

Thus the quantity of the product depends (apart from duration) on the product of a series of terms, one for each preceding link in the chain, and each consisting of the ratio of the constructive rate constant to the total rate constant for transformation of the substrate in question. In case the substance itself is being transformed or lost, the reciprocal of the total rate constant for these processes constitutes another term.

Consider now the relation of variation in a product (Y, dropping primes) to variation in a catalyst (X) re-

sponsible in part for one of the transformations. The rate constant x varies directly with the quantity of catalyst. Using c only for the rate constant additional to x,

$$Y = Y_\infty \left(\frac{x+c}{x+c+d}\right) \tag{3}$$

The curve expressing the relation of (Y) to (X) is a hyperbola, asymptotic at its upper limit ($Y\infty$). Doubling the quantity of x will less than double the amount of product. There should be some approach to dominance of the active phase of the gene and the greater the activity the closer the approach to complete dominance. It is convenient to measure dominance in this case by the ratio of the excess of the positive homozygote over the heterozygote to its excess over the other homozygote.

$$\frac{Y_{AA} - Y_{Aa}}{Y_{AA} - Y_{aa}} = \left(\frac{X_{AA} - X_{Aa}}{X_{AA} - X_{aa}}\right)\left(1 - \frac{X_{Aa} - X_{aa}}{X_{Aa} + c + d}\right) \tag{4}$$

From this it will be seen that there is an approach to a linear relation only if the increase in the rate constant due to one dose of the catalyst ($X_{Aa} - X_{aa}$) is small compared with the total rate constant ($X_{Aa} + c + d$) for disposal of the substrate, while there is an approach to complete dominance if the transformation largely depends on the positive phase of the gene (X_{aa}, c, d all small, compared with X_{Aa}).

If the gene (X) catalyzes a destructive process as far as the product in question is concerned

$$Y \propto \frac{c}{x+c+d} \tag{5}$$

The relation between character and catalyst is again represented by a hyperbola, but one descending toward a lower asymptote with increasing amount of the catalyst. The formula for degree of dominance comes out exactly the same as before. A gene with this mode of action will appear as an incompletely dominant inhibitor of the character in question.

If a second catalytic action intervenes between the primary catalyst and the product (Fig. 4), the relation is

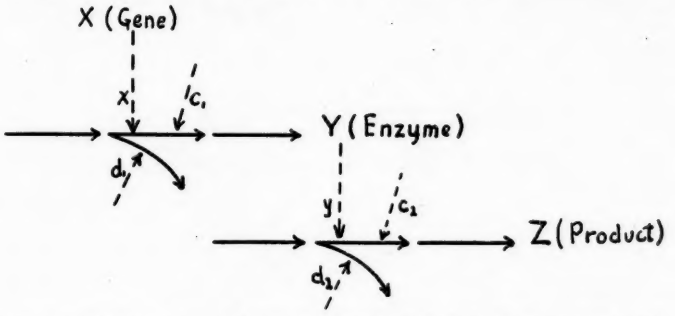

FIG. 4. Relation of gene action to amount of enzyme, as primary product, and of this to amount of secondary product.

still hyperbolic, irrespective of whether both catalytic actions are constructive, both destructive, or differ in this respect.

$$Z \propto \frac{y + c_2}{y + c_2 + d_2} \quad \text{or} \quad \frac{c_2}{y + c_2 + d_2}$$

depending on whether the action of Y is constructive or destructive in relation to Z.

$$Y \propto \frac{x + c_1}{x + c_1 + d_1} \quad \text{or} \quad \frac{c_1}{x + c_1 + d_1}$$

Measuring dominance as before

$$\frac{Z_{AA} - Z_{Aa}}{Z_{AA} - Z_{aa}} = \left(\frac{X_{AA} - X_{Aa}}{X_{AA} - X_{aa}}\right)\left(1 - \frac{Y_{Aa} - Y_{aa}}{Y_{Aa} + c_2 + d_2}\right)\left(1 - \frac{X_{Ac} - X_{ca}}{X_{Ac} + c_1 + d_1}\right) \qquad (6)$$

If X acts constructively on production of Y, Z exhibits greater dominance of the active phase of X than does Y. If, however, X acts destructively on Y, X exhibits less dominance than does Y, the most extreme case being that in which c_2 and d_2 approach zero. Even in this case the heterozygote can not fall below intermediacy in relation to the active phase of X.

A bimolecular reaction may intervene between gene and product. In Fig. 5, Z is a joint product of B and M.

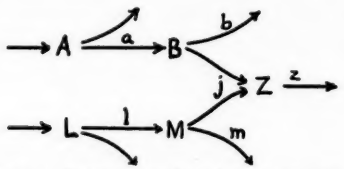

FIG. 5. Diagram of bimolecular reaction.

The rate constant (j) for this reaction being rate per unit mass of B and M jointly is of the dimensions of a reciprocal quantity.

Equations of flux equilibrium

$$\frac{dB}{dt} = aA - bB - jMB = 0$$

$$\frac{dM}{dt} = lL - mM - jMB = 0$$

$$\frac{dZ}{dt} = jMB - zZ = 0$$

Values for B, M and Z can be found directly in terms of A and L. Two extreme cases are of most interest. If B and M are largely disposed of in other ways than by formation of Z $\left(\frac{mb}{j}\right.$ large compared with aA and $\left.lL\right)$ the solutions are approximately

$$M = \frac{lL}{m}\left[1 - \frac{aAj}{mb}\right] \text{ or even } \frac{lL}{m} \tag{7}$$

$$B = \frac{aA}{b}\left[1 - \frac{lLj}{mb}\right] \text{ or even } \frac{aA}{b} \tag{8}$$

$$Z = \frac{aAlLj}{zmb} \tag{9}$$

The dominance relations of B and M to genes acting on processes back of them are of course approximately as if there were no combination to form Z, while the dominance relations of Z to genes acting on either chain are approximately as if these were combined in one chain under the preceding theory.

If Z is, on the contrary, produced almost quantitatively from the more limited component $\left(\frac{mb}{j}\right.$ smaller than aA

and lL) the approximate solution is as follows, taking aA > lL:

$$B = \frac{aA - lL}{b} \tag{10}$$

$$M = \frac{blL}{jaA} \tag{11}$$

$$Z = \frac{lL}{z} \tag{12}$$

The amounts of M and its products other than Z are negligible. For B and its products (other than Z) there is the interesting possibility of a reversal of dominance of active genes in the chain leading to B. The production of Z, limited as it is by that of M, subtracts from that of B, giving a threshold for the latter. If B falls below M in the heterozygote of such a gene, but exceeds M in the homozygote, the inactive phase would appear to be completely dominant over the active phase. The dominance of the gene for albinism (c^a) in certain combinations in the guinea-pig (c^dc^dff pale cream, c^dc^aff, c^ac^aff white) has been interpreted in this way (Wright, 1927).

Another interesting consequence of this mechanism is that inactivation of the more abundant component may release the products of the less abundant component. B behaves as an inhibitor for M and *vice versa*. There is here a possible mechanism for such antagonistic reactions as Goldschmidt finds indicated in his intersexes in Lymantria.

As for Z and later derivations, its quantity depends on that of the more limited component (M) as if it were the product of a monomolecular reaction and the dominance relation to genes in this series are thus the same as in the latter case. But while minor variations back of the more abundant component (B) are without effect, such a reduction at any link that aA becomes less than lL reverses the situation. Thus complete or nearly complete inactivation of a gene necessary to the progress of the reaction toward B will behave as a practically complete recessive to the active phase.

Several bimolecular reactions may intervene between gene and product. The active phase will completely dominate over the inactive phase if at any one of these reactions the gene in question is back of the more concentrated component. The increased tendency toward dominance of the active phase of genes through this mechanism much more than overweighs the possibility of reversal of dominance by the special condition discussed in a preceding paragraph.

So far as it has been assumed that rate of transformation varies jointly with the concentration of substrate and enzyme. This has been found to apply at low concentrations of both, but in general requires qualification (Waldschmidt-Leitz, 1929; Haldane, 1930b). It appears that the rate of transformation varies in such a way as to indicate dependence on the concentration of a compound of the substrate with the enzyme. The reaction must thus in general be treated as involving a bimolecular one between substrate and enzyme and a diagram such as the following (Fig. 6) should be substituted for Fig. 4.

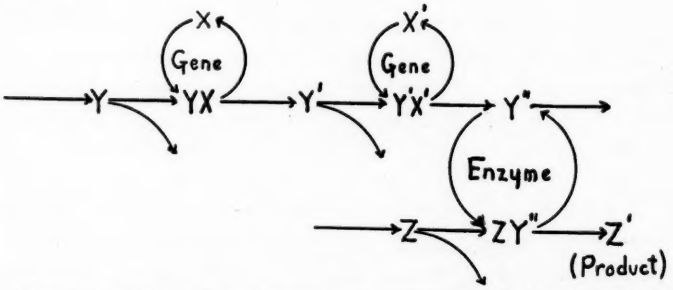

FIG. 6. Relations of gene to enzyme as primary product and of this to secondary product, treating gene and enzyme as entering into temporary combination with their substrates.

For our present purpose it is only necessary to consider the extreme cases. That in which the compound is low in amount compared with both components gives the theory already discussed. If the total catalyst (X + YX)

is in excess, but most of the substrate is always in combination, further increase in the catalyst can have no effect and all genes necessary for the production of the catalyst should exhibit complete dominance above a certain level. If, on the other hand, the substrate is in excess while the gene itself as a catalyst, or a catalyst directly controlled by it, is kept continually in combination, the gene would exhibit intermediacy in its phases. Such a case as that of the gene affecting yellow endosperm in corn, demonstrated by Mangelsdorf and Fraps (1931) to exhibit exact proportionality of effect (measured as vitamin A content) to number of positive genes (yyy, Yyy, YYy and YYY) might come here. Conversely, a gene necessary for any step in the formation of the substrate would tend to exhibit complete dominance.

Multiple Allelomorphs

The interpretation of multiple allelomorphic series as often representing different grades of activation of a gene is an obvious extension of this theory of dominance. Fig. 7 illustrates the numerical relations under the two extreme forms of the theory.

The dominance phenomena are somewhat different. Under the theory of proportionality of rate to substrate and catalyst jointly, the higher allelomorphs should show increasing degrees of dominance over the completely inactive phase (or indeed over any particular lower allelomorph) but absolutely complete dominance is theoretically never reached. Under the theory of control of rate by the limiting factor, there is exact intermediacy of heterozygotes (up to a certain level), then a range of increasing dominance of the higher allelomorph until at a certain level complete dominance is attained. The general observation that the highest member of a series shows most complete dominance is in harmony with both theories, although the apparent completeness of dominance often found accords best with the limitation theory.

Considering the series of heterozygotes between a given higher member and successively lower members,

the two theories give opposite expectations. With a hyperbolic relation, there is maximum dominance (by formula 4) over the lowest allelomorph. Under the limitation theory, there is *least* dominance in this case (if dominance is present at all, but is not complete). Cases are known which definitely accord with the limitation hypothesis in this respect. In guinea-pigs the gene C seems to be completely dominant over all its allelomorphs ex-

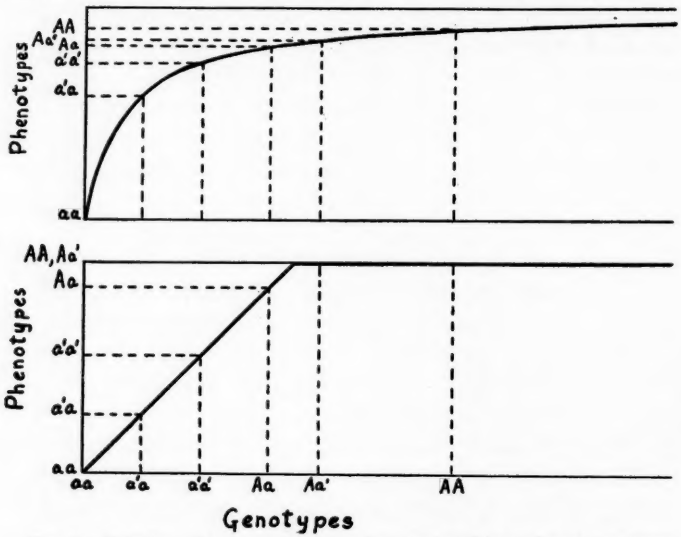

FIG. 7. Relation of gene activity to phenotypic effect under two extreme hypotheses: above, on theory that reaction varies jointly with gene activity and amount of substrate; below, on theory that the reaction varies only with that component (gene or substrate) which is most limited in amount.

cept the lowest, c^a, but Cc^a (in the presence of gene pp) shows intermediacy. The situation is the same in the mouse (Snell, 1931). Cases of partially dominant effects of complete loss (deficiency) may also be explained in this way.

It must be remembered in this connection that the theory of joint control and of limiting factors are not really separate theories but merely extreme cases of a single theory. Some examples may require one, some the

other and yet others an intermediate case of the general theory.

All-or-None Reactions

The condition of flux equilibrium has been assumed as characteristic of vital phenomena over considerable periods of time. But developmental processes must have a beginning and an end. As already noted, it has been demonstrated in several cases that genes may affect a character by advancing one or the other of these processes and such mechanisms would seem of necessity to be of first importance in morphogenesis.

This does not necessarily wholly change the relation of dominance to gene activity, since as Goldschmidt especially has emphasized such effects probably trace to differences in rates. Graded effects of delay in onset or termination should thus be functions of underlying rates. However, mere quantitative differences in the duration of an elementary process are likely to have consequences of an all-or-none character, making dominance (if not already shown by the elementary process) a largely accidental matter in relation to gene activity. If the termination of one process occurs after another has begun with one homozygote, but occurs before, with the alternative homozygote, it is largely chance (from the present standpoint) whether the heterozygote occurs before or after.

Modifying Factors

The relative frequency of complete dominance in cases of genes with major and minor effects is a question of great importance. Most of the direct evidence of dominance naturally comes from genes with major effects. Genes with minor effects are largely a deduction from the statistical phenomena of quantitative variation following crosses.

In so far as genes are related to characters through catalyzed reactions whose rates vary jointly with both substrate and catalyst (hyperbolic theory) the smaller the difference in the catalyst, the less the dominance (for-

mulae 4 and 6). Under this theory, minor factors should rarely exhibit dominance.

In the case in which reaction rate depends only on the limiting factor, the situation is more mixed. Minor variations back of the limiting factor exhibit intermediacy. On the other hand minor variations back of a component only slightly in excess are more likely to show complete recessiveness than larger variations. Where there is a larger factor of safety small variations, however, will have no effect.

In the more general case, between the above extremes, minor variations tend to have intermediate heterozygotes.

If an all-or-none reaction intervenes, the heterozygotes of major variations are likely to fall invariably on one or the other side of the threshold, giving complete dominance or recessiveness. The effects of minor variations tend to be confused by those of other modifying factors, including environment, and the effects of the alternative homozygotes are manifested merely in differences in percentage of occurrence, with heterozygotes showing an intermediate percentage. On the whole it appears that an approach to complete dominance or recessiveness should be expected more of factors with major than with minor effects.

The evidence from crosses between strain shown to differ in multiple minor factors is, I believe, in harmony with the view that lack of dominance is the rule for such factors. It may be noted that only slight departures from intermediacy of individual heterozygotes need be postulated to account for lack of intermediacy of F_1 or even for an excess development of F_1 over both parents (if these are not at opposite extremes and if there is any correlation between direction of deviation from exact intermediacy and direction of effect).

DIRECT EVIDENCE IN NATURE OF DOMINANCE

The argument for the prevailing dominance of the active phase of factors with major effects has been based

here largely on theoretical grounds. I will not go far into detail on the observations which indicate the actual occurrence of such a relation. The superficial correlation between dominance and positive effect is familiar and formed one of the bulwarks of the old presence and absence hypothesis. Thus presence of pigment is usually dominant over absence. But the occurrence of definite exceptions such as dominant whites was an embarrassing fact, It is, therefore, of especial significance that where physiological analysis of characters is pushed back a step, such exceptions tend to disappear. From the work on extracts from the skins of mammals of different genetic constitution it has come out that in those cases in which the dominant phase is more pigmented, the extract from the dominant contains an enzyme which is merely absent (or reduced in effectiveness) in the recessive phase. There is no antienzyme present in the latter. On the other hand, in those exceptional cases in which the dominant is less pigmented, the extract has been shown to possess the property of inhibiting the action of extracts from colored skin.

The blood groups of man (Bernstein, 1925) depend primarily on 3 allelomorphic genes of the interesting type which can not be arranged in a quantitative series with respect to effect. They also appear to have no adaptive significance. It is significant therefore to find that agglutinogen A is dominant over its absence (Group O), agglutinogen B is dominant over its absence (also Group O). The heterozygote between the two positive agglutinogens shows both. In the heterozygotes each gene dominates in its positive effect. This seems to be the rule in non-linear multiple allelomorphic series. A woman who carries the recessive gene for the "red blind" type of color blindness in one X chromosome and that for the "green blind" type in the other, has normal vision, but all her sons are of one or the other type (Waaler, 1927). A similar situation holds for the scute locus in *Drosophila* (Agol, 1931). The phenomena of pseudo-

dominance of recessive genes in organisms heterozygous for deficiencies in the locus in question indicates that the dominant gene is a positive entity (Mohr, 1923). In *Drosophila,* allelomorphs of white eye, heterozygous for a deficiency in the same locus, resemble the combinations of these allelomorphs with white eye itself. "Exaggeration" of the recessive effect in heterozygous deficiencies calls to mind the tendency toward incomplete dominance of type over extreme inactivation discussed on a previous page.

Perhaps the most direct evidence comes from the experiments of Stern (1929) and of Muller, League and Offermann (1931). Stern showed that the piling up of Y chromosomes containing "bobbed bristle" causes, not more extreme development of the character bobbed bristles, but normal type. Muller and his coworkers, following x-ray treatment, caused an accumulation of small fragments of chromosomes carrying particular recessive genes. In general there was approach to wild type indicating that the genes (hypomorphs) behaved like type genes of low activity. In a few cases there was increasing divergence from type with increase in number of genes. But these "neomorphs" were largely semi-dominants. Their occurrence does not invalidate the hypothesis that the ordinary recessive mutations represent partial or complete inactivation.

PART III. REINTERPRETATION OF STATISTICAL PRINCIPLES

STATISTICAL RESULTS OF GENE PHYSIOLOGY

Let us return now to the statistical phenomena of dominance. Such considerations as the above (as far as available) led me several years ago (1929a) to suggest that "in the hypothesis that mutations are most frequently in the direction of inactivation and that for physiological reasons, inactivation should generally behave as recessive, at least among factors with major effects, may be

found the explanation of the prevalence of recessiveness among observed mutations."

Ford (1930) has objected as follows: "The only explanation of dominance previous to the publication of Dr. Fisher's theory was the long-discussed physical one of partial or complete loss (or inactivation) of genic material at mutation, and Professor Sewall Wright falls back upon this in his criticism of it. Not only does the loss hypothesis lead to an evolutionary impasse when accepted as a general principle, but it can not be too strongly urged that as such it is untenable in the face of the proved fact of reverse mutation."

Ford here seems to imply that the loss and inactivation theories are equivalent. There are many ways of inactivating a complex mechanism such as a motor car (and probably also a gene). The momentary effect on progress is the same as that of complete loss, but the ultimate outlook is not so hopeless. More to the point perhaps is the fact that enzymes can be inactivated by addition of certain substances and completely reactivated by later treatment. I see no difficulty in holding that variegated corn possesses an inactivated gene which reverts to activity by mutation thousands of times in the same corn plant.

With respect to the supposed evolutionary impasse, the objection applies only if it be supposed that all mutation is of the nature of inactivation. This I explicitly avoided. There seems little reason to believe that the rare major mutations, whose prevailing recessiveness was the object of discussion, are representative of the mutations which are of evolutionary significance. The latter are probably as a rule ones with minor effects and thus often semidominant over the previous type gene, but still dominant over complete inactivation. In any case genes with increased or new activities are probably as likely to be seized upon as those with reduced activity, even though the latter be much more numerous.

EFFECTS OF SELECTION

However, I have no objection to an evolutionary process by which the dominance of wild type over mutations may be increased provided the pressure toward fixation is sufficient to be effective. Plunkett[2] (1932a, b) has recently pointed out that the direct selection of a type, subject to variation from numerous minor genetic and environmental factors, would tend to build up a factor of safety against such variation and automatically against mutations, irrespective of their past occurrence.

He calls attention to the well-known fact that wild type is much less susceptible to variation from such factors (*e.g.*, temperature) than are mutations and explains this as due to "differences in the distance of the developmental process from its asymptote at the time it ends: processes controlled by wild type genes usually closely approach their asymptotes, while those modified by mutant genes may be terminated by the effects of other developmental processes while still very incomplete." This theory seems quite in harmony with that which I presented. From the standpoint of the present paper, we are probably concerned here with those genes which have to do with the timing of processes whose dominance was found to be largely a matter of chance from the physiological standpoint and by this very fact easily subject to natural selection. Any one who has worked with genes whose effects are subject to threshold effects (*e.g.*, white spotting) is familiar with the ease with which the dominance of these can be changed by introduction of modifiers.

EVOLUTIONARY IMPLICATIONS

From the standpoint of the theory of dominance it may seem of little importance which mechanism is accepted if it be granted that selection has been an important factor. This is not at all the case, however, with the impli-

[2] Essentially the same view-point was also presented by Muller at a meeting of the 6th International Genetics Congress in 1932, but unfortunately did not reach publication until after the above was written.

cation of Fisher's and Plunkett's selection theories, for the theory of evolution. Fisher used the observed frequency of dominance as evidence for his conception of evolution as a process under complete control of selection pressure, however small the magnitude of the latter.

My interest in his theory of dominance was based in part on the fact that I had reached a very different conception of evolution (1931) and one to which his theory of dominance seemed fatal if correct. As I saw it, selection could exercise only a loose control over the momentary evolutionary trend of populations. A large part of the differentiation of local races and even of species was held to be due to the cumulative effects of accidents of sampling in populations of limited size. Adaptive advance was attributed more to intergroup than intragroup selection.

Plunkett's theory of dominance as an incident to the building up of a factor of safety of wild type against variation in general seems wholly compatible with such a view of evolution. It may be noted that intergroup as well as intragroup selection would be effective here.

GENERAL CONCLUSIONS

As a rule the most active phase of a gene with major effects is dominant over less active phases, as a result of physiological relations, allied to the law of diminishing returns, applying to its own activity or to that of primary or secondary products.

Incomplete dominance implies that variations of the gene and its successive products leading to the observed character *all* affect the limiting components in the reactions into which they enter or at least components which are not in excess. Genes with minor effects (so called modifiers) are especially likely to fall in this class.

If there is still incomplete dominance at a stage in the reaction chain at which an all-or-none reaction intervenes, dominance of a gene comes to depend on the effects of independent modifiers and in this case is without rela-

tion to its primary activity. On the other hand, dominance in this case is likely to depend on evolutionary history, specifically to the building up of a factor of safety for the most adaptive type of the species.

The measurement of dominance as an element in the study of the effects of gene substitutions in every possible genetic and environmental background furnishes one of the most useful tools in tracing the genetic physiology of characters.

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THE AUTOCATALYTIC GROWTH-CURVE

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THE usual argument for the Robertson theory of autocatalytic growth depends on the fact that the growth-curves of many organisms or populations of organisms can be represented by equations of the type which describe certain kinds of autocatalytic chemical reactions:

$$dx/dt = K(B-x)\,(A-x) \qquad (1)$$

where

$$B < x < A.$$

The integral form can be written

$$\ln \frac{(x-B)}{(A-x)} = K(B-A)\,(t-t_1) \qquad (2)$$

or

$$x = \frac{Ae^{K(B-A)\,(t-t_1)} + B}{1 + e^{K(B-A)\,(t-t_1)}}. \qquad (3)$$

Setting $B = 0$ gives the original form of Robertson,[1] which is also the well-known logistic; as the equation stands we have the modified form of Robertson,[2] or that of Crozier.[3] (The identity of these two modifications has been shown by Titus.[4]) It is the purpose of this paper to consider the nature of the curve and discuss the argument from a mathematical view-point.

Both the function of (3) and the generalized logistic of Pearl and Reed[5] are essentially the familiar hyperbolic tangent. This fact has been generally overlooked by users of the curves. We shall show the relation for the autocatalytic equation; the proof for Pearl and Reed's generalization is similar.

[1] T. B. Robertson, *Roux' Archiv.*, 25: 581, 1908.
[2] T. B. Robertson, *Jour. Gen. Physiol.*, 8: 463, 1926; 12: 329, 1929.
[3] W. J. Crozier, *Jour. Gen. Physiol.*, 10: 53, 1926.
[4] H. W. Titus, *Jour. Wash. Acad. Sci.*, 20: 357, 1930.
[5] R. Pearl and L. J. Reed, *Metron.*, 3: no. 1, 1923.

The hyperbolic tangent is defined as follows:

$$\tanh z = \frac{e^z - e^{-z}}{e^z + e^{-z}}. \tag{4}$$

For simplicity set

$$K(B-A) = 2k,$$

then from (3)

$$x - B = \frac{(A-B)e^{2k(t-t_1)}}{1+e^{2k(t-t_1)}},$$

$$\frac{x-B}{A-B} = \frac{e^{2k(t-t_1)}}{1+e^{2k(t-t_1)}}$$

and

$$\frac{x-B}{A-B} - \tfrac{1}{2} = \frac{e^{2k(t-t_1)}-1}{2[1+e^{2k(t-t_1)}]},$$

Multiplying numerator and denominator of the right hand side by $e^{-k(t-t_1)}$

$$\frac{x-B}{A-B} - \tfrac{1}{2} = \tfrac{1}{2}\frac{e^{k(t-t_1)} - e^{-k(t-t_1)}}{e^{k(t-t_1)} + e^{-k(t-t_1)}}$$

$$= \tfrac{1}{2}\tanh k(t-t_1)$$

by (4). Then

$$x = \frac{A+B}{2} + \frac{A-B}{2}\tanh k(t-t_1). \tag{5}$$

The generalized logistic of Pearl and Reed[5] can similarly be reduced to the form

$$x = \frac{A}{2} + \frac{A}{2}\tanh f(t). \tag{6}$$

The following properties of the autocatalytic function, some of them already mentioned in the literature, are easily deduced from the well-known characteristics of the hyperbolic tangent.

1. Slope, or absolute growth-rate, is given by

$$dx/dt = \tfrac{1}{2}k(A-B)\operatorname{sech}^2 k(t-t_1)$$

$$= \frac{k(A-B)}{2\cosh^2 k(t-t_1)}. \tag{7}$$

Values are easily calculated with the aid of common tables of log cosh.[6]

2. The curve lies between two horizontal asymptotes, $x = A$ and $x = B$. (*cf.* Titus.)[4]
3. It is symmetrical with respect to its point of inflection, which falls at $t = t_1$, $x = \frac{1}{2}(A+B)$.
4. When $B < 0$, so that the lower asymptote is below the axis, the significant part of the curve, that above the axis, has a non-symmetrical appearance. Speaking only of this portion it is proper to say that the point of inflection occurs when less than half the maximum height has been attained. (*cf.* Titus.)

[6] Smithsonian Mathematical Tables. Hyperbolic Functions. 1909.

In this case the curve has a positive slope as it crosses the axis. A rigid interpretation of the theory thus would call for the rather interesting but unlikely phenomenon of spontaneous generation of living from non-living matter.

5. For $B=0$ we have the logistic, or simple autocatalytic curve, with midpoint at half the height.
6. Curve-fitting and the calculation of values of x are sometimes simpler from (5) than from (2) or (3) since tables of the hyperbolic functions and their logarithms can be employed.[6] For this work it is better to write

$$x = C + D \tanh k(t - t_1) \qquad (5a)$$

and

$$dx/dt = kD/\cosh^2 k(t - t_1). \qquad (7a)$$

The fact that an experimental curve of growth can be fitted very well by a curve of the autocatalytic type is sometimes advanced as evidence in favor of the Robertson autocatalytic theory. To investigate the validity of this argument, let us look into the possibilities of the autocatalytic function.

A curve of a given type can always be fitted very closely to curves of mathematically very different nature. As an illustration suppose that we are watching a worker studying the growth of an organism whose true law, unknown to him, is essentially the probability integral:

$$x = 1 + \frac{2}{\sqrt{\pi}} \int e^{-x^2} dx.$$

We shall suppose him endowed with such accuracy that he makes no experimental error, so that he obtains the values marked "observed" in the table. From them he plots the points indicated by small circles in Fig. 1. On looking at his graph he sees that it is asymptotic to the t-axis, and to the line $x = 2$; that it has a point of inflection at half its height, and is symmetrical with respect to this point. These are all characteristics of a simple autocatalytic curve. So he fits the autocatalytic curve to his data by least squares or some other method and gets, let us say, the logistic

$$x = 1 + \tanh (1.2t)$$

Using a table of the hyperbolic tangent he computes the "Calculated" values and from them draws the broken-line curve of Fig. 1. As we see, it fits quite well. If he follows precedent he will doubtless conclude that the growth of the organism is indeed autocatalytic. Yet no

mathematician would say what this amounts to, that the probability integral is a form of the hyperbolic tangent. (For a comparison of these two curves, the reader should consult a recent paper by Winsor.[7])

This hypothetical example illustrates the mathematical fact that *the fitting of an autocatalytic curve to a set of plotted points is absolutely not a proof that the law governing the location of those points was the law of autocatalysis.*

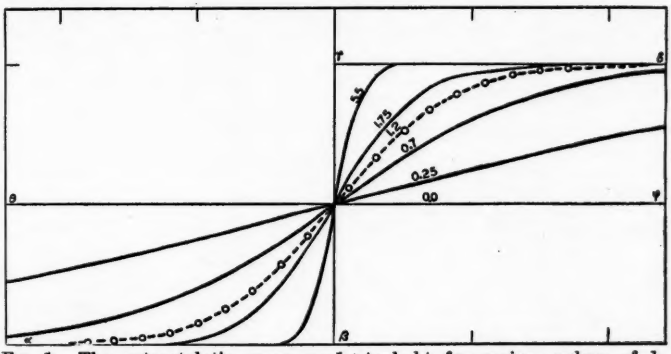

FIG. 1. The autocatalytic curve, $x = 1 + \tanh kt$ for various values of k. The case $k = 1.2$, shown by the dotted lines, fits the curve of the probability integral, which points are marked by small circles.

It may be thought that while the "fitability" of one or two curves might be due to coincidence of this sort, the fitting of the large number of curves that appear in the literature can hardly be explained on such a basis, but rather gives a strong probability to the theory of autocatalysis. With this idea in mind let us see how varied a set of figures the autocatalytic function can produce.

We shall limit ourselves to the simple logistic by setting $B = 0$ in (5) or $D = C$ in (5a), and thus not deal with the changes in the significant part of the curve which result from an asymptote below the axis. We also put $t_1 = 0$, since this does not alter the shape but only determines the instant from which we begin to measure time. The equation then becomes

$$x = C + C \tanh kt.$$

[7] C. P. Winsor, *Jour. Wash. Acad. Sci.*, 22: 73, 1932.

First let us hold C constant at 1 and assign various values to k. For $k = 0$ we have the straight line $\theta\psi$, Fig. 1. As k increases, the familiar S-shape appears, shown for $k = 0.25$ and 0.7, $k = 1.2$ gives the curve our experimenter fitted to his observations, and when k becomes indefinitely great the logistic actually approximates the broken line $\alpha\beta\gamma\delta$.

Now hold $k = 0.7$ and observe the variation for changing C. This set is of curves shown in Fig. 2. When

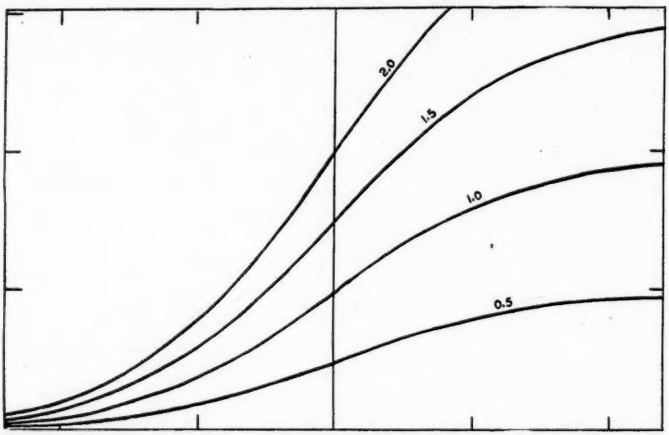

FIG. 2. The autocatalytic curve, $x = C + C \tanh 0.7t$ for various values of C. When $C = 1$ the curve is that for $k = 0.7$ of Fig. 1.

$C = 0$ the autocatalytic curve is the t-axis. As C increases, the curvilinear form is gradually assumed, the slope for any value of t becomes steeper, and the maximum height increases. The curve marked $C = 1$ is the one for $k = 0.7$ in Fig. 1.

These illustrations show only a few of the members of the autocatalytic family. It should be realized that for every curve in the infinite set of Fig. 1 there is a complete infinite set like that of Fig. 2. In addition there are the apparent change in shape and lowering of the inflection point in the significant part that result when the lower asymptote is below the axis. With such a wealth of form it is not to be wondered at that the "autocatalytic curve" can be made to fit a wide variety of data.

Summary

The "curve of autocatalytic growth" (and also the generalized logistic) is essentially the hyperbolic tangent. Use of this fact simplifies the theoretical and practical handling of the equation.

Demonstration of a good fit of the autocatalytic curve to a given growth-curve is *no proof* that the growth is autocatalytic, since the autocatalytic curve can be made to fit curves of similar appearance but very different nature. The variety of forms which the autocatalytic curve can assume is evidence of the futility of such an attempted proof.

THE GROWTH OF A HYPOTHETICAL ORGANISM

TIME t	"OBSERVED" x	"CALCULATED" x
−1.8	0.01091	0.02625
−1.6	0.02365	0.04208
−1.4	0.04771	0.06714
−1.2	0.08969	0.10630
−1.0	0.15730	0.16635
−0.8	0.25790	0.25572
−0.6	0.39614	0.38309
−0.4	0.57161	0.55376
−0.2	0.77730	0.76450
0.0	1.00000	1.00000
0.1	1.11246	1.11943
0.3	1.32863	1.34521
0.5	1.52050	1.53705
0.7	1.67780	1.68581
0.9	1.79691	1.79320
1.1	1.88021	1.86678
1.3	1.93401	1.91542
1.5	1.96611	1.94681
1.7	1.98379	1.96675

NOTE.—Fitting the equation. When, as is the simple logistic, $C = D$ from (5a) and (7a) the point of inflection is at $t = t_i$ and $x = D$ and $dx/dt = kD$. Determine the slope at this point, *e.g.* with a tangent meter (Richards and Roope, *Science*, 71: 290, 1930), graphically or by computation and then $k =$ slope/D. If necessary, an improved fit may be obtained by changing these values slightly. Two approximations usually give a very good fit. This method is of special value when the upper limiting assymptote is not precisely known.

A FURTHER TEST SHOWING THE DOMINANCE OF SELF-FERTILITY TO SELF-STERILITY IN SHEPHERD'S PURSE[1]

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IN studying self-sterility in shepherd's-purse, it is important to consider the behavior of crosses between the self-sterile species *Capsella* (*Bursa*) *grandiflora* and any one of the three self-fertile species which belong to the same chromosome group. Shull (1923) showed that when *Capsella Viguieri* was used as the male parent, fully fertile hybrids resulted. A further study between self-sterile and self-fertile species (Shull, 1929) indicated that self-sterility segregated out in the F_2 as a recessive trait in a monohybrid Mendelian ratio.

Further studies were conducted along this line by Dr. Shull, E. K. Hall and myself. A full report of this work has not been published, but certain observations have been noted (Riley, 1932). Several crosses were made between *Capsella grandiflora* and the other three species, and the F_1 hybrids were both perfectly fertile and completely self-compatible. Both self-fertile and self-sterile plants appeared in the F_2, but the ratio of the one to the other was not 3:1. The nearest approach to it was found in one family which produced 117 self-fertile and 57 self-sterile plants, or a 2.1:1 ratio, but in the majority of cases the ratio was from 1.5 to 1.8:1. As these data did not seem conclusive of anything, I decided to repeat the work later.

Seed from crosses made by Dr. Shull between two *Capsella grandiflora* plants used as females and *C. rubella* and *C. tuscaloosae* as males were raised as I have re-

[1] The work reported in this paper was done in the greenhouse at Princeton University during the year 1931–32, when the author held a Charlotte Elizabeth Procter fellowship.

ported, and the F_1 generations were found to be self-fertile. One F_2 family from one of the F_1 hybrids between *C. grandiflora* and *C. rubella* split exactly 3:1. Three F_2 families of hybrids between the other *C. grandiflora* plant and *C. rubella* gave a 3:1 ratio. When six F_1 plants from one of the *C. grandiflora* × *C. tuscaloosae* crosses were selfed, three F_2 families resulted which approximated the 3:1 ratio, while the other three were close to 2:1. Of three F_2 families from the other *C. grandiflora* mated with a plant of the species *C. tuscaloosae,* one contained exactly three self-fertiles to one self-sterile, one split exactly 2:1, and the other was very close to the latter ratio.

An original cross between *C. grandiflora* and a segregate between *C. grandiflora* and *C. Viguieri* yielded eight self-fertile and twelve self-sterile plants. It was concluded that the segregate used as a male parent was heterozygous for self-fertility. Three plants of the F_1 gave an F_2 generation of which two families split 3:1 while the other was more akin to 2:1.

It may be argued that the populations were not of sufficient size to ensure a 3:1 ratio in all cases where it might be expected, although between 50 and 100 plants were raised in most families. This is probably true, but in the light of the previous results obtained by Shull, Riley and Hall, it was deemed advisable to continue this study for another generation. An F_3 was raised with the expectation that if 3:1 were the true situation in the F_2, one third of the F_3 plants should breed true to self-fertility, while the remainder would segregate. Ten F_3 families were raised from ten self-fertile plants from the F_2 family, v5, and six of these split into self-fertiles and self-steriles, while the other four were completely self-fertile. A similar study of seven F_3 families from the F_2 family, r7, showed that two were entirely self-fertile, while the remaining five segregated. Since the publication of this work, it was called to my attention that both F_2 families which had been tested in the F_3 happened to

be ones which gave a 3:1 ratio rather than 2:1. This still left open the possibility that some F_2 families might split 3:1, while others might be 2:1. Although this did not seem probable, I decided to test the point of raising an F_3 from one of the families which split approximately into two self-fertiles to one self-sterile.

The F_2 family, t11, arose from selfed seed of plant t4(5), a self-fertile F_1 plant from a cross *C. grandiflora* × *C. tuscaloosae*. Family t11 split into 32 self-fertile and 18 self-sterile plants. The expected 3:1 ratio is 38:12, while the expected 2:1 would be 33:17, so it is clear that family t11 was nearer the latter.

Eight self-fertile plants of family t11 were bagged and allowed to set seed, and eight F_3 families were raised from them. As can be seen from Table 1, five of these families split into self-fertiles and self-steriles, while the other three families were composed entirely of self-sterile

TABLE 1

AN F_3 GENERATION FROM A CROSS, *Capsella grandiflora* × *C. tuscaloosae*

Family	Origin	Self-fertile plants	Self-sterile plants
t28	t11(2) × self	35	13
t29	t11(16) × self	34	12
t30	t11(22) × self	49	0
t31	t11(25) × self	50	0
t32	t11(26) × self	48	0
t33	t11(28) × self	44	5
t34	t11(34) × self	14	15
t35	t11(35) × self	33	13

All self-fertile = 3.
Splitting = 5.

plants. Since an F_2 family which seemed to segregate 2:1 produced an F_3 generation in which five families split and three were self-fertile, it seems conclusive that 3:1 represents the true nature of the F_2 generation of crosses between self-sterile and self-fertile Capsella plants.

The peculiar ratios found by Shull, Hall and myself in earlier unpublished studies may not necessarily indicate any true difference in the nature of the material used at

the two different times, but may rather be ascribed to errors of classification made by the two junior authors, who did much of this work when rather unfamiliar with the material. It is not always easy to classify one of these hybrids as self-fertile or self-sterile, especially when it has not been guarded from insects. Many plants were found with a large number of enlarged capsules, but with about as many sterile ones as well. There was a tendency to regard these plants, when unbagged, as self-sterile and to consider that the high percentage of enlarged capsules was due to insect visitors. More recent investigations, however, lead one to suspect that these plants are actually self-fertile. During the past year, I counted the fertile and sterile capsules upon a large number of plants and found many plants in which the number of both types of capsule was approximately equal. For example, on one F_3 hybrid there were 242 fertile and 155 sterile capsules. During the earlier work, such plants would probably have been regarded as self-sterile; but it is hardly likely that insects could have accounted for that unusually large number of fertile capsules. About thirty plants of this same family were bagged, and the flowers were allowed to pollinate themselves undisturbed under the bag. In some cases, not a single capsule enlarged, leaving no doubt that the plant was self-sterile. In other instances, however, there were large numbers of both fertile and sterile capsules upon a plant, typical ratios being 67:163, 70:46 and 90:66. Since insects were excluded, there can be no doubt that self-fertilization produced these full capsules, and it is difficult to regard as self-sterile a plant upon which there were over fifty inflated capsules, full of good, viable seeds. Many of the sterile capsules upon plants of shepherd's-purse can be accounted for by "proximal sterility," a situation mentioned by Shull (1929) in which the lower flowers of the central axis set no seed. The cause of this proximal sterility is unknown, but it is a feature quite characteristic of many species of Capsella. If the sterile capsules

which are sterile because of proximal sterility are eliminated from the tabulation of fertile and sterile capsules, the proportion of fertile ones on a self-fertile plant becomes much higher. Proximal sterility does not account for all the undeveloped capsules, however, for in studying the racemes of many of these hybrids, both bagged and unguarded, one notices sterile capsules, either singly or in groups up to six or eight, distributed at random among fertile capsules. It is probable that in our earlier work, fertile capsules upon such plants were considered as due to insects, while the many undeveloped capsules, due to proximal sterility or other causes, were regarded as indicating that the plants were self-sterile. Later results upon bagged plants, however, show that the fertile capsules are normal and that the plants are probably self-fertile, although not in as high a degree as is often found. This later work seems to indicate that many plants formerly classed as self-sterile were really self-fertile and that errors of classification account for the unusual ratios of self-fertiles to self-steriles obtained in the preliminary investigation. As no data in regard to the number of enlarged and sterile capsules upon these early plants were kept, this work unfortunately can not be rechecked. Later results, however, lead to the conclusion that self-fertility is a simple Mendelian dominant to self-sterility in the *rubella* group of the genus Capsella.

In conclusion, I would like to express my sincere appreciation to Dr. Geo. H. Shull for introducing me to the study of self-sterility in Capsella, for his ready willingness to give advice and, above all, for the benefit which comes of daily contact with a ceaseless worker in his laboratory.

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THE GENETICS SOCIETY OF AMERICA

PAPERS READ AT THE CHICAGO MEETING

PROFESSOR P. W. WHITING
SECRETARY

1. *The Nuclear Cycle and Factorial Segregation in Homothallism:* J. E. SASS, Iowa State College. In *Coprinus sterquilinus* the basidia and other hymenial cells are binucleate. Nuclear fusion takes place in the basidium, followed by two divisions of the fusion nucleus. Four sterigmata and spores are formed on each basidium. A nucleus migrates from the basidium into each spore and immediately undergoes division. There are indications of at least one more nuclear division within the spore. It is probable that at least some of the mature spores contain more than two nuclei. The germ tube contains a variable and increasing number of nuclei, and develops into a branched non-septate, multinucleate mycelium. There is no indication of dikaryons or conjugate mitoses, and there are no clamp connections. Each cell of the mycelium may contain from one to many nuclei. The terminal cells in particular contain many nuclei. Two or three days after germination, there appear on the periphery of the mycelium, stout, rapidly growing hyphae having binucleate cells and clamp connections. By tracing these "secondary" hyphae back into the mycelium they are found to arise in a region where there is abundant anastomosing between cells containing one to several nuclei. Fruit bodies are produced in such monosporous cultures. This nuclear cycle appears to be identical with the cycle associated with heterothallism, at least with respect to two critical points, *i.e.,* nuclear fusion in the basidium and the ultimate restoration of the dikaryophase. The occurrence of karyogamy implies subsequent numerical reduction of chromosomes. This reduction can be accepted without the evidence of chromosome counts, which, in this species, are unsatisfactory. The time and place of chromosome reduction concerns us only in so far as numerical reduction is presumably associated with the segregation of genetic factors (4). In view of the fact that each spore of *C. sterquilinus* receives, in one nucleus, all factors necessary for fruiting, it follows that segregation of the factors concerned does not occur during the two nuclear divisions in the basidium.

2. *Tetraploid Maize:* L. F. RANDOLPH, U. S. Department of Agriculture and Cornell University. Tetraploidy is unknown in normal stocks of maize but may be induced readily by intermittent heat treatments of the proembryo, as previously described. Diploid maize has 20 somatic chromosomes, and the derived tetraploids have 40 somatic chromosomes. A corresponding increase in nuclear and cell size accompanies the doubling of the chromosomes. These changes have a marked influence on the plant as a whole and cause the tetraploid to be morphologically and genetically distinct from the parental diploid. Tetraploid seedlings differ from diploid seedlings in having larger, more widely spaced stomates and thicker leaves. At maturity the tetraploids in comparison with related diploids have larger stalks, broader and thicker leaves and tassels and floral parts of increased size. Tetraploids produce abundant viable pollen, which is distinctly larger than the pollen of diploids. When self-pollinated or intercrossed the tetraploids are highly fertile, except for occasional partially sterile types apparently similar to those induced in diploids by the heat treatments. Maize tetraploids do not breed true for chromosome number because of an irregular type of chromosome pairing. Plants with one or a few chromosomes more or less than the typical number occur not infrequently in tetraploid progenies. This variation in chromosome number appears to have no appreciable effect upon vigor or growth habit, since inbred tetraploid strains are very uniform. Strains of tetraploid maize are highly cross-sterile with diploid strains in both direct and reciprocal crosses. Triploids and very rarely tetraploids are produced from such crosses but with a very low frequency. Mixtures of approximately equal amounts of pollen from 2N and 4N plants were applied to the silks of both pollen parents. In the cross $2N \times 2N + 4N$ the pollen from the diploid functioned almost to the exclusion of the pollen from the tetraploid and produced well-filled ears of diploid seed. The reciprocal cross $4N \times 2N + 4N$ gave a very high per cent. of aborted grains identical with those produced in the cross $4N \times 2N$ and a low per cent. of tetraploid seed derived from the pollen of the tetraploid seed parent. Abundant pollen was used in these crosses. The results obtained from these controlled pollinations were confirmed in an isolated mixed planting of open-pollinated tetraploids and diploids in which the hybrid seed could be identified genetically.

3. *Segregation of Quantitative Genes in Tetraploid Tomato Hybrids as Evidence for Dominance Relations of Size Characters:* E. W. LINDSTROM, Iowa State College. The decapitation-callus technique with tomatoes, permitting a direct comparison of 2n and 4n progenies arising from the same F_1 plant, affords critical data on the nature of gene segregation involving quantitative characters, such as fruit size and shape. Using the most fertile tetraploid—from the cross of the wild *Lycopersicum pimpinellifolium* by the domesticated *L. esculentum* species—comparisons of the 4n and 2n F_2 progenies proved that the 2n distribution possessed a significantly larger standard deviation and coefficient of variability. While the modes of the two curves were identical, the mean of the 2n F_2 was significantly larger, resulting in a typical skewed (positive) curve for the 2n material and a nearly normal curve for the 4n progeny. This is interpreted to mean a dominance of the small, fruit-size genes instead of a geometric effect of such genes, despite the fact that the 2n F_2 distribution when plotted logarithmically approaches a normal curve. The skewness of the diploid F_2 accordingly is caused by the emergence of the recessive, large-size genes which do not emerge with such frequency in the 4n progeny. Even with maximum chromatid segregation only 4.6 per cent. recessives appear for a single tetrasomic set of chromosomes. If universal, this dominance bias is a critical example of the recessive nature of size genes in domesticated forms in contrast to the dominance of their wild allelomorphs.

4. *The Relation of Nuclear Content to Cell Size in the Polyploid Series of Datura stramonium:* E. W. SINNOTT, Columbia University, A. F. BLAKESLEE, Carnegie Institution of Washington, Cold Spring Harbor, N. Y., and HELEN HOUGHTALING, Barnard College. In most of the tissues of the flower stalk there is a rather close approach to direct proportionality between chromosome number and cell volume, the values for diploid, triploid and tetraploid being approximately two, three and four times as great as for haploid. In the leaf, however, the increase in cell volume from the lower to the higher members of the series is far greater than the increase in chromosome number. In the fundamental tissue of the petiole, for example, the values for diploid, triploid and tetraploid are approximately three, nine and twenty-seven times that of haploid, indicating that the proportionality is here a geometric rather than an arithmetic one.

5. *Chromosome Numbers in Habrobracon:* MAGNHILD TORVIK-GREB, University of Pittsburgh. Cytological study indicates that there are 10 chromosomes in the normal haploid male and 20 in both the normal diploid female and the biparental diploid male. Spermatogonial and secondary spermatocyte counts were made in the male; oögonial counts in the female. Both haploid and diploid males show an abortive first maturation division, while the second maturation division is apparently equational in both. The two cells resulting from the second maturation division metamorphose into mature sperm cells.

6. *Selective Fertilization and Sex-Determination in Hymenoptera:* P. W. WHITING, Carnegie Institution of Washington, Cold Spring Harbor, N. Y. The discovery of a sex-linked factor, fused, in Habrobracon demonstrates the truth of the theory recently advanced (*Biol. Bull.*, 65: 357–358) that females are X + Y + 2A, haploid males either X + A or Y + A and diploid males either 2X + 2A or 2Y + 2A. Heterosyngamy gives rise to females, while homoeosyngamy gives rise to diploid males. A fused male, fu.X, mated with his heterozygous daughters, fu.X/Fu.Y, sires females wild-type (straights), fu.X/Fu.Y and about 4 per cent. fused (crossovers), fu.X/fu.Y. Certain other fused males, fu.Y, mated with similar females sire fused (straights), fu.Y/fu.X, and about 9 per cent. wild-type (crossovers), fu.Y/Fu.X. (The difference in percentage of crossovers is due to viability.) Thus it is demonstrated that the four expected types of ova are produced—straights, Fu.Y and fu.X, and crossovers, fu.Y and Fu.X. Homoeosyngamy fails to occur, unless the gametes are from closely related stock. Selective fertilization is demonstrated genetically.

7. *A Gene for Intersexuality in Drosophila virilis:* G. A. LEBEDEFF, Carnegie Institution of Washington, Cold Spring Harbor, N. Y. A third chromosome recessive gene was found which transforms homozygous females into intersexes and in extreme cases into almost normal males. The gene has no effect on males, as is shown by the segregation in an inbred line, from which cultures giving 4:3:1 as well as 2:1:1 ratio of normal males, females and intersexes were obtained. This was further proved by the fact that from crosses between vermilion females (sex-linked gene) and wild type males, both carrying gene for intersexuality, only males were vermilion but the females and

intersexes were of the wild type. Morphologically intersexes are of four rather distinct types: (1) Almost normal females, but which often have rudiments of male external genitalia and frequently ovaries transformed into ovo-testes. (2) Hermaphrodites which have two sets of male and female internal and external genitalia. Gonads of hermaphrodites in most cases are ovo-testes attached to both duct systems; in a few cases gonads of both sexes are present. (3) Intersexes of the male type but which still have female shape of the body due to the presence of one extra tergite. (4) Almost normal males with one or both undersized testes. After selection through several generations four lines have been isolated giving predominantly one of the described types of intersexes, indicating that modifiers, probably few in number, determine the type of intersexes.

8. *Genes and Inductors of Sex Differentiation in Amphibians:* EMIL WITSCHI, State University of Iowa. Experiments on the genetics and the embryology of sex differentiation will be presented that lead to the following conclusions: (1) There is no direct interaction between the male and female sex genes. (2) These genes independently determine the development of separate inductors of testicular and ovarial differentiation. (3) Male and female inductors act as antagonists. (4) The inductive activity appears a short time before visible morphological sex differentiation and it assumes different quantitative values according to developmental age, size of inductor, size of the supplied area, distance between inductor and receptor and other developmental factors. (5) The ultimate sex of an individual is not determined directly by genic balance but by the interaction of inductors which are far removed from and only partly determined by the sex genes.

9. *Interaction of the Inductors of Sex Differentiation in Heterogeneous Parabiotic Twins of Newts and Salamanders:* EMIL WITSCHI, State University of Iowa. Embryos of different urodeles have been grafted together in the following combinations: *Amblystoma tigrinum—A. maculatum; A. tigrinum—A. jeffersonianum; Amblystoma—Triturus.* In all combinations the first member is larger and reaches the stage of sexual differentiation earlier than the second one. In heterosexual combinations the interactions as expressed by gonad structure in the twins are strikingly different, according to whether the first or

the second member is of the male sex. The varied results permit an analysis of the inductive processes in the involved species.

10. *The Interaction of the Genes Bar and Vestigial in Drosophila:* OTTO S. MARGOLIS, Washington Square College, New York, N. Y. The effect of the gene vestigial on facet number in bar eye of Drosophila was investigated by comparing facet numbers in Bar and Bar vestigial flies. Since vestigial is known to increase the length of the egg-larval period, some effect on facet number was anticipated. Vestigial produced a slight decrease in facet numbers in both males and females over a range of temperatures from 13.7° C. to 31° C. At temperatures below 20° C., the temperature-facet curves tend to converge, so that the effect of vestigial at low temperatures, though probably real, is not statistically significant at one or two points. The temperature-effective period for facet determination was studied at 28° C. by making transfers of larvae from 28° C. to 22° C. at successive intervals of one to two hours. This period was found to be somewhat longer for Bar vestigial than for Bar. In previous determinations of the temperature-effective period, individual variability in the beginning and end of the period has not been taken into consideration. Consequently, the values obtained for the length of the period are too great, and do not give an adequate measure of the mean value for the population. A method for evaluating the mean length of the temperature-effective period, based upon the distributions of facet numbers in the various transfer groups, is presented.

11. *The Temperature Effective Period in Development of "Eyeless" in Habrobracon:* B. R. SPEICHER, Carnegie Institution of Washington, Cold Spring Harbor, N. Y. The recessive factor eyeless produces a pair of large lateral lobes on the head bearing minute compound eyes. The tissue giving rise to this region is produced by a pair of imaginal disks which appear at the beginning of the last larval stadium and undergo rapid growth near the close of the same period. Occasional ("non-lobed") wasps show the lobes united over the head and less pronounced; these individuals are more common in cultures reared at low temperatures. Eyeless cultures transferred during development from 23° C. to 30° C., or from 30° C. to 23° C., show proportions of non-lobed wasps characteristic of the temperature at which the wasps matured, if the transfer was made before

close of the last larval stage. Otherwise, the cultures show proportions of non-lobed wasps characteristic of the temperature originally applied. The critical temperature effective period thus coincides with the period of most rapid growth of the tissue forming the affected structures. The ratio of non-lobed among total eyeless in cultures transferred after hatching of the eggs is varied from the expected by a slight effect of the original temperature, indicating a second and less effective period during embryogeny.

12. *The Effects of Temperature on the Mutants dimorphos and vestigial in D. melanogaster:* MORRIS HENRY HARNLY and MARIE LÉCUYER HARNLY, Washington Square College, New York, N. Y. Dimorphos (dm), a sex-linked recessive mutation modifying the expression of the vestigial gene, appeared in the inbred vestigial stock used for determining the temperature effective periods and growth curves of the vestigial wings. At 25° C. the wings of the homozygous dimorphos vestigial males resemble strap, having a mean length of 1.70 mm, and are practically identical with homozygous not dimorphos vestigial males reared at 31° C. The wings of the homozygous dimorphos vestigial females reared at 25° C. are "vestigial" in appearance, though measurements show them to be somewhat larger than those of the non-dimorphos vestigial females reared at the same temperature. The effects of temperature during complete development on the dimorphos vestigial combination have been examined at twelve points over a range of seventeen degrees centigrade. In the flies reared below 25° C. there was some decrease in the mean length of the wings in the males but none in the females. Flies reared between 25° and 32° C. had larger wings, the change appearing in the males at lower temperatures than in the females. The two sexes attained equal wing lengths at 31° C. and wing areas at 32° C. At the latter temperature there was no sexual dimorphism, the wings were nearly wild type in appearance and an occasional "normal" wing was obtained in both sexes. The "critical temperature" previously described for vestigial males and females was absent in the males of this dimorphos-vestigial combination; but it was observed at a lower temperature in the females.

13. *An Analysis of the Temperature-Effective Period of the Ocellar Bristle in Scute 1 of Drosophila melanogaster:* GEORGE

P. CHILD, New York University (now at University of Minnesota). The temperature-effective periods of the various bristles affected by scute 1 were determined in the usual manner under carefully controlled genetic and environmental conditions. This method of determining the temperature-effective period gives the limits of the period for the whole population being studied, *i.e.*, the period from the time at which the first flies start to be affected by temperature to the time at which this effect has been completed in all the flies. The temperature-effective period as measured is, therefore, the sum of two quantities: the mean duration of the temperature-effective period in the individual flies, and the variation from fly to fly in the time at which their temperature-effective periods are reached. By an analysis of the left-right correlation of the bristles of flies transferred during the temperature-effective period and by experimental determinations of the numbers of flies in a transfer group which have entered and which have passed through their temperature-effective periods at the time of transfer, the temperature-effective period of the ocellar bristle in the individual fly has been determined as not less than 5.2 per cent. and not more than 7.5 per cent. of the egg-larval period, with a most probable value (on the basis of the available data) of 5.4 per cent.; the temperature-effective period in any one fly lies entirely between the time at which 89.3 per cent. and the time at 96.8 per cent. of the egg-larval development has been completed. However rough these values may be, they represent the first attempt to determine the actual duration and location of a temperature-effective period in the individual organisms, all previous determinations giving merely the limits of this period for a group of individuals.

14. *On the Determination of Genetic Constants of Relative Growths:* A. H. HERSH and M. J. FELDSTEIN, Western Reserve University. In the application of the relative growth function the constants have been determined for the most part graphically. Where a high degree of genetic control makes it feasible to undertake the estimation of the differences in the constants of relative growth brought about by a relatively small genetic difference, the method of least squares is clearly to be preferred. The fitting of a curve to data by this latter method may be carried out in two ways: (1) in terms of the arithmetic values of the variables x and y and so the fit is to the equation, $y = bx^k$, or (2) in terms of the logarithmic values, in which case the fit

is to the equation, $\log y = \log b + k \log x$. The first method is based on the theoretical y^2 – weight correlation, while the second is the familiar regression method. A comparison is made of the results obtained by applying these two methods to data on facet number in the dorsal and ventral lobes of the eye in males and females of fifteen genetically diverse stocks of bar-eyed Drosophila. The two methods give somewhat different results, but no certain criterion is established as yet for deciding which of the two methods is to be preferred.

15. *Genes in the First Chromosome of the Tomato As Related to Time of Fruit Ripening:* T. M. CURRENCE, Minnesota Agricultural Experiment Station, St. Paul. By crossing a late plant homozygous recessive for the first chromosome genes, d p o s, with an early plant homozygous D P O S, and back-crossing the F_1 to the recessive parent it was found that genes in this chromosome cause a difference of 19 ± 0.85 days in the time of ripening fruit. Data on the different single crossovers suggest that factors affecting earliness are located in the regions of d p and s. The o region did not appear to have any marked effect on time of ripening. The gene or genes in the D region hastened maturity approximately nine days. The D and P regions together hastened the ripening of fruit 14 days. The S region had a variable effect in the presence of different combinations of the other factors. The d p o S plants were 10 days earlier than those with all the recessives, but the all-dominant group was but four days earlier than the group recessive only for s. Apparently this region has a diminishing effect when combined with other genes for earliness. The double and triple crossovers were too few in numbers to be used for drawing conclusions. The association found to exist may be due to linkage or they may be multiple effects of the marker genes.

16. *Fruit Size Effects of Qualitative Genes in the Tomato:* J. W. MACARTHUR, University of Toronto. There is some hope of properly analyzing quantitative (*e.g.*, size) inheritance, if Mendelian methods are substituted for the Galtonian technique, and the most favorable materials are selected (those with great size range, known cytology, and each chromosome marked by one or more qualitative genes). Earlier experiments on size of body, ears, flowers, cobs, seeds have usually started with crosses of parents differing slightly, as 2:1 or 4:1; tomato varieties exist

with fruit size differences as great as 80:1 or even 200:1, and with qualitative genes located in each of 10 of the 12 chromosomes. Study of fruit weights of all F_2 and B.C. plants in 18 crosses shows that qualitative genes, whether with or without shape effects, often also exert characteristic size effects. Thus *l* (lutescent) retards maturity by two weeks and reduces fruit weight by 30 per cent.; *o* elongates and narrows the fruit and reduces its weight by half; peach increases fruit weight slightly and *f* (fasciated) increases locule and seed number and fruit width, and increases weight 60 per cent. Many genes (*d, r, y, c, h, u*) are nearly neutral in size effect and exhibit linkage with "size genes" in chromosomes I, II, III, IV and VII. The "multiple factors" for size are apparently usually dominant or recessive (not blending), and often very unequal (not polymeric) in effect; and size genes as such may not exist except as one of the many effects of other genes.

17. *Modification of Stumpy Legs of Habrobracon:* RAYMOND J. GREB, University of Pittsburgh. An analysis was made of the legs of 150 stumpy males and 170 males mosaic for stumpy to determine the amount of and the direction of modification, as well as the genetic constitution of the modified tissue in mosaic individuals. Legs were graded, according to the number of atypical tarsal segments present, as grade 0, 1, 2, etc., through 5. Of the 150 stumpy individuals examined, only 32 had legs that graded above zero. The 103 such legs graded: 57—one, 35—two, 10—three and only 1—four. The 170 mosaics for stumpy had 167 atypical legs: 69—one, 44—two, 22—three, 11—four and 21—five. In order to determine whether both wild-type and the mutant tissue were modified, the factor, honey body color, was added. Of the 27 males mosaic for stumpy and honey, four showed wild-type legs and legs of classes 4 or 5 similarly pigmented, while legs otherwise pigmented were typically stumpy or only slightly modified. These gave evidence that wild-type tissue as well as stumpy tissue may be modified. The atypical legs were graded on the basis of their position with respect to type. Legs were more frequently and more extremely modified when type was present on the same side of the body than when it was present only on the opposite side.

18. *Fertile Mosaics in Drosophila:* C. P. OLIVER, University of Minnesota. Among offspring of treated Drosophilas appeared

some fertile mosaics. One breeding gynandromorph was heterozygous for scute, vermilion, forked, carnation and star. On the left side, the mosaic was female throughout. On the right side, the front leg, eye, wing and abdomen were male. The abdomen was twisted towards the male side, but external genitals were female. All sex-linked characters were expressed in every expected part on the male side, except that the right scutellars were present and the eye was carnation, not the expected vermilion-carnation combination. Either vermilion failed to appear with the other eye red, or only part of the treated normal X was lost. The mosaic bred as a female, fertility decreasing considerably after the tenth day. Its sixty offspring included no sex-aberrants. Apparently no translocation involving the X with II or III had been induced. The gynandromorph heterozygous for treated star produced males normal for sex-linked characters without star more frequently than with star. Similar results were found with mated offspring of the mosaic. Crossing over between the sex chromosomes of the mosaic occurred with the normal frequencies in so far as could be determined from the small numbers. Another mosaic minute on the left thorax produced among normal and minute offspring a female with only the right thorax mutant. A mosaic with only the right eye rough gave through four generations a few individuals with only one eye rough.

19. *A New Type of Cytological Map of the X-chromosome in Drosophila melanogaster:* T. S. PAINTER, University of Texas. From a study of the normal morphology of the X-chromosome and of breaks of a known genetic character, in the salivary glands of larvae, a new type of cytological map has been made. Since the various regions of the X have distinct morphological patterns, we have for the first time a qualitative cytological method of chromosome analysis. The approximate morphological positions of 22 gene loci, scattered well along the X, have been plotted. It has been found (1) that while in the left-hand end of the X-chromosome the morphological map is longer than the crossover value would indicate, from crossveinless on to the right there is good agreement between crossover value and morphological position. Thus, a break between forked (62.0) and Bar (62.2) morphologically is about 59 units from the left-hand end. The right-hand morphological limit of miniature (42.8) is about 38 units from the left end. (2) The inert region of the X is

not present in any form as yet identified in the nucleus. Either it has been eliminated in ontogeny, or is present in some unrecognized form. (3) The only part of the Y-chromosome found, so far, is part of a segment which morphologically is similar to and pairs with that portion of the X which carries the normal allelomorph for bobbed.

20. *A Cytological Study of Short Deficiencies in the X-chromosome of Drosophila melanogaster:* OTTO MACKENSEN, University of Texas (introduced by T. S. Painter). Using Painter's method of studying salivary gland chromosomes, a cytological analysis is being made of short deficiencies, of known genetic character in the X-chromosome. When a normal and a deficient X unite in somatic synapsis they pair up line for line, except in the deficient region where the normal chromosome buckles. This enables one to determine in the most detailed way how much is missing morphologically from the deficient element. It is found that genetic deficiencies may be accompanied by the loss of definite bands and areas of the X-chromosome. For example, in the stock known as "Notch 8," which shows genetically the absence of the loci for white, facet and abnormal abdominal sclerites, certain bands of the "facet area" are always absent. This study is of interest first, since it definitely proves that genetic deficiencies may be accompanied by cytological deficiencies, and second, because it enables us to determine the cytological locus of genes more exactly than the usual translocation method.

21. *Induced Crossing Over in the Male Cells of Drosophila:* J. T. PATTERSON and META L. SUCHE, University of Texas. We have carried out a series of experiments designed to induce by x-radiation crossing-over in the males of *Drosophila melanogaster*. To accomplish this, male larvae, heterozygous for a series of eight mutant genes in the III-chromosome, were x-rayed and the F_1 males then back-crossed to females having this same series of recessive genes. The F_2 cultures yielded seventy-seven variants, out of a total of 8,371 flies, that could be assigned to the effects of x-rays. Genetic tests showed that a majority of these cases were due to an exchange of segments between the homologous III-chromosomes. Such tests further showed that 80 per cent. of the cases were viable in the homozygous condition. Crossover tests gave approximately normal crossover values for the regions

affected by the induced crossing over. The conclusion is reached that x-radiation induces crossing over in the male when applied to immature germ cells which contain the diploid number of chromosomes. The effect is much more marked when the treatment is given during the growth stage of the spermatocyte that corresponds to the stage in the female germ cell when normal crossing-over is supposed to occur. The complete paper will appear in *Genetics*.

22. *Duplication 33e27 in Drosophila hydei:* WARREN P. SPENCER, College of Wooster. This spontaneous duplication was found in a female from a single mating culture of *sc* ♂ to $\frac{w}{c \quad sc}$ ♀. By tests it has been found to contain the genes $+^{w}$– I, 81.3, sc– I, 84.6 and $+^{v}$– I, 94.2, but not $+^{m}$– I, 47. It is not yet known whether it carries bb – I, 140.5. The duplication is lethal in males and somewhat inviable in females. It is marked phenotypically by a plexate venation which is particularly concentrated about the posterior cross-vein. The plexate character varies from very extreme forms to those with no extra veins. The latter are distinguished by failure of one or more longitudinal veins to reach the margin. This duplication gives independent assortment with cherry, miniature, white and vermilion loci of the x-chromosome and with scarlet II, 0.0, orange III, 0.0 and squatty IV, 49.7. The presence of the mutant, scute 33a14, in the duplication makes possible a study of that gene in triploid, diploid and haploid combinations. In duplication sc, $\frac{sc}{sc}$ certain bristles, such as or^{1}, are sometimes found, whereas they are always absent in $\frac{sc}{sc}$ and sc combinations. One $+^{sc}$ gene is dominant over two sc genes under standard environmental conditions.

23. *Comparative Investigations on the Reduction Division:* EDWARD C. JEFFREY, Harvard University. It is beyond question that the phenomena of meiosis constitute at present the most unsatisfactory chapter in general works on cytology. This situation is apparently due to two causes. Firstly, the conclusions reached are very generally mainly the result of compilation rather than of actual comparative observations. This situation is responsible for many and hopeless contradictions. Secondly,

the objects chosen are those with large and conspicuous chromosomes during meiosis. A wide series of investigations, covering a considerable length of time and including plants as well as animals, has made it clear that those forms in which the chromatin in the meiotic stages is not too abundant present the most favorable conditions for the critical observation of the essential features of the extremely important reduction division. Very favorable objects for such investigations are supplied by many families of the Dicotyledones and by the Conifers. It is apparently clear in these groups that the nuclear filament emerges from the resting condition as a continuous spireme, as has been maintained by many distinguished cytologists in the past. This is at first very slender (leptotaene, leptonema). Later masses of chromatin in the reproductive or haploid number make their appearance at intervals in the fundamental substance (linin) of the now thicker spireme. Such masses have been very frequently described as prochromosomes or chromocenters, etc., by other observers. They must, however, in view of their nature and development be chromosomes proper. These later undergo longitudinal division, and this condition is also frequently to be observed in the linin matrix of the spireme. In the metaphase of meiosis, these pairs, at first strung out end to end in the spireme, become separated from each other and are arranged vertically to the plane of the metaphase plate. If the observations here summarized are correct, and no pains have been spared to place them on a sound and broad basis, many of the chromosomal hypotheses at present accepted must be fundamentally revised. This is, for example, notably the case with the hypothesis of chromosomal pairing (Synapsis, syndesis) in meiosis, so generally adopted at the present time. The views here defined have the advantage, by no means unimportant, of instituting a complete parallelism between the essential feature of karyokinesis in both somatic and reproductive cells. The only essential difference lies in the number of chromosomes into which the continuous spireme is segmented. These are twice as numerous in the somatic as in the reproductive divisions.

24. *Chromosome Fragmentation and Other Phenomena of Meiosis in Species and Species Hybrids of Paeonia:* G. L. STEBBINS, JR., Colgate University. Chromosome fragmentation at meiosis has been observed in *Paeonia lutea, P. Veitchi, P. Woodwardi, P. tenuifolia, P. Mlokosewitschi, P. corsica, P. triternata,*

P. tomentosa, in horticultural varieties of *P. suffruticosa, P. albiflora* and *P. officinalis,* var. *lobata,* and in the F_1 hybrids *P. lutea* × *suffruticosa, P. Veitchi* × *Woodwardi, P. Veitchi* × *albiflora, P. tenuifolia* × *albiflora, P. albiflora* × *tomentosa,* and *P. officinalis* var. *lobata* × *albiflora.* The fragments are either a part of a single chromatid, parts of two sister chromatids or the entire portion of a chromosome distal to the spindle fiber attachment. The fragments may be broken off in the prophase, the early heterotypic anaphase or the homeotypic anaphase. They are usually extruded into the cytoplasm and may form extra nuclei and pollen grains, of which the nucleus is smaller than a single chromosome. Some of the direct causes of fragmentation are crossing-over in bivalents heterozygous for an inversion, twisting of chromatids at the heterotypic metaphase and the formation of constrictions during the anaphase separation. The relation between the percentage of fragmentation and that of other abnormalities, as well as chiasma frequency, is discussed. Fragmentation is most common in species that are members of a polymorphic complex and is usually greater in F_1 hybrids than in their parents. Evidence from the pairing of bivalents heterozygous for a deficiency or a deletion, and from interlocking of both homologous and non-homologous chromatids in Paeonia favors the chiasmatype theory of crossing-over.

25. *Chiasmata in Melanoplus femur-rubrum:* E. MARIE HEARNE and C. LEONARD HUSKINS, McGill University. Chiasma frequencies in *Melanoplus* show no significant reduction between early diplotene and metaphase. Compensating chiasmata occur twice as frequently as non-compensating. Among the former, interlocked and non-interlocked chromatids occur with equal frequency. The observations are therefore opposed to Sax's theory of crossing-over. They are in accord with the general "partial chiasmatype" hypothesis. The preponderance of compensating chiasmata indicates a type of genetic interference not met with in Drosophila, and Belling's latest formulation of his theory of crossing-over requires modification to fit the observations for this animal in which there is both "chromatid interference" and "chiasma interference." Terminal chiasmata arise from earlier interstitial ones, but the movements of chiasmata prior to metaphase are sometimes towards the spindle attachment. Darlington's chiasma theory of metaphase pairing requires extension to fit certain configurations. Chromosomes of different length con-

tract differentially, and a greater degree of contraction occurs in the spermatagonial divisions than at meiosis. A "tertiary" split occurs at late diakinesis. These observations are opposed to Darlington's "precocity theory" of meiosis. A heteromorphic bivalent behaves in conformity with expectation in the partial chiasmatype hypothesis.

26. *Chromosome Structure in Trillium erectum:* C. LEONARD HUSKINS and STANLEY G. SMITH, McGill University. The leptotene chromosomes of Trillium are single threads without trace of splitting. Twists which appear to be correlated with the later formation of chiasmata can be seen at zygotene and pachytene. The "secondary" split begins in late pachytene, but is not completed until after opening-out has occurred along the primary or synaptic plane. Coiling of chromonemata begins at early diakinesis, and from the middle of this phase on the course of the four chromatids can be traced clearly. During diakinesis the four chromatids are spiralled, except at the attachment constriction where they lie parallel in pairs. The reduction in number of chiasmata prior to anaphase is very slight. Cancellation of chiasmata, without terminalization, sometimes occurs. During late diakinesis a "tertiary" split occurs in each of the four coiled chromonemata. Changes in the direction of coiling, which appear to be correlated with earlier chiasma formation and with crossing-over, are readily observed at anaphase. The homeotypic division follows without further splitting of the chromonemata. The "tertiary" split of late diakinesis functions as the plane of separation at the first pollen grain mitosis. The observations are discussed in relation to crossing-over and the mechanism of chromosome behavior in mitosis and meiosis.

27. *Heteromorphic Homologous Chromosomes of Wheat Considered in Relation to the Chiasmatype and Classical Hypotheses:* C. LEONARD HUSKINS and JANE D. SPIER, McGill University. Three heteromorphic pairs of homologous chromosomes differing in degree of inequality distal to the spindle attachment were chosen for comparative study. The first had one member broken off immediately adjacent to the attachment. If paired, the chromosomes segregated reductionally at the first division in all cases. They were paired in 56 nuclei and unpaired in 34 nuclei examined. The second pair had one member lacking approximately half of the distal arm. Thirty-five reductional and four

equational first division separations were observed. The third pair was similar to the second but had a slightly greater discrepancy in size of the unequal arms. Thirty-one reductional and 11 equational first division separations were observed, and in six nuclei the unequal homologues were unpaired. These observations are in accord with the general partial chiasmatype hypothesis and with the chiasma theory of metaphase pairing. They can be accounted for on the "classical" theory only if association of non-sister strands at the attachment is assumed; the first pair provides evidence against this possibility in the present case.

28. *Chromosomal Interchanges in Maize: Reduction of Crossing-over and the Association of Non-homologous Parts:* CHAS. R. BURNHAM, Osborn Botanical Laboratory, Yale University. In plants heterozygous for an interchange of a terminal piece of the short arm of chromosome 9 with a small terminal piece of the long arm of chromosome 5, about 2 per cent. of recombination between the point of interchange and waxy and about 8 per cent. with shrunken were observed. Tests in plants homozygous for the interchange show that the order in the short arm is *spindle fiber – interchange – wx – sh*. In plants heterozygous for the interchange, yellow green–2 and shrunken gave 11, shrunken and waxy gave 6 per cent.; the values in normal stocks being 23 and 20 per cent., respectively. The greatest reduction is in the region nearest the point of breakage. Cytological study of mid-prophase figures at meiosis in such plants shows wide variation in the position of the "cross," with usually a close association of the parts. Since there was only one point of interchange in each chromosome, all the positions of the "cross" but one involve the association of non-homologous parts. If crossing-over occurs only when homologous parts are together, the observed reduction is explainable. In chromosome 5, red aleurone (*pr*) gave 25 per cent., while brown midrib–1 gave 47 per cent. of recombination with the break. These are more remote genetically from the interchange point than the most remote gene tested in chromosome 9. Similar behavior was observed in the 2–6 interchange previously reported. Another interchange is characterized by marked stability at mid-prophase and does not show a reduction in crossing-over. When genes in both the interchanged and non-interchanged pieces in both chromosomes were involved simultaneously, the observed recombination values can only be

fitted into a cross-shaped linkage map, the point of intersection being the point of interchange.

29. *Linkage Relations of Certain Factors and Their Serial Order in Chromosome 5 in Maize:* CHAS. R. BURNHAM, Osborn Botanical Laboratory, Yale University. Three-point backcross linkage tests of: yellow stripe (ys_1), red aleurone (pr) and brittle endosperm (bt); and of pr, brevis (bv) and brown midrib (bm_1); and F_2 tests of bt with bm, show the order and percentages of recombination to be: ys_1 8 pr 17 bv 5 bm_1. The gene bt is very close to bm_1 (less than 1 per cent. recombination), but the order is unknown. The tests with virescent (v_2), with one exception, indicate that v_2 is on the ys_1 side of pr. The one exception is in an F_2 segregating for bv as well as v_2 and bm_1 and apparently is due to poor viability. Backcross tests of v_2 with bv, F_2 tests of v_2 with bt and with bm_1, gave independence which would not be expected if v_2 is on the bm_1 side of pr (since pr–v_2 show 42 per cent. of recombination). In a 5–7 interchange, pr and the interchange point gave 15 per cent. recombination, while bm_1 gave 46 per cent. Three-point tests with pr, v_2 showed that the break is between them, v_2 and the break giving 14 per cent. recombination. The order therefore is $v_2 - interchange - pr - bm_1$. Cytologically, the break in chromosome 5 occurred toward the end of the long arm near the subterminal knob. In a 5–6 interchange, the break is also on the long arm of chromosome 5 but is near the middle of the chromosome not far from the insertion. The recombination value with pr was 17 per cent., that with bm_1 was less than 1 per cent. The combined genetical and cytological data presented above indicate that the order of the genes, in going from the end of the long arm toward the shorter arm, is: $v_2 - ys_1 - pr - bv - bm_1$ with v_2 probably very close to the end of the longer arm.

30. *The Behavior of the Extra Chromosomes in Black Mexican Inbreds and F_1 Hybrids with Dent Types of Maize:* L. M. HUMPHREY, Iowa State College. An examination of 11, 8-year-old inbred lines of Black Mexican sweet corn, in which no effort had been made to select for any particular chromosome number, showed extra chromosomes in every case. The number of extra chromosomes ranged from 2 to 10. Variability was noted within lines. The extra chromosomes do not appear to be fragments. In mitosis their behavior is entirely normal, indicating that

spindle fiber attachments are actually present. In meiosis at pachytene and subsequent stages a weakness of pairing is evident. At diakinesis and metaphase the extra chromosomes are in the form of both bivalents and univalents. They behave irregularly at anaphase with subsequent irregularities in the number of chromosomes distributed to the microspores. Behavior in the F_1's is the same where extra chromosomes are present in pairs. Where only a single extra chromosome is present it behaves as a typical univalent.

31. *Summary of Ten-Year Records of the Breeding Behavior of Primary and Secondary 2n+1 Types in Datura:* A. F. BLAKESLEE and A. G. AVERY, Carnegie Institution of Washington, Cold Spring Harbor, N. Y. Records on nearly 50,000 field-grown offspring of 12 primary and 14 secondary (2n + 1) types lead to the following conclusions: (1) Both primaries and secondaries differ widely in viability (transmission of the extra chromosome to their offspring). The highest viability is shown by 2n + 23 · 24, with 33.4 per cent. transmission, and the lowest by 2n + 19 · 20, with 3.0 per cent. transmission. (2) The number of primaries thrown by their own secondaries also varies widely even when percentages are corrected for viability. This fact indicates that disjunctions responsible for 1n + 1 primary gametes are not at random. (3) The number of secondaries thrown by unrelated primaries is extremely small (0.035 per cent.). The number of secondaries thrown by their own primaries is slightly larger (0.088 per cent.). (4) There is a marked difference in respect to the number of new mutations of unrelated 2n + 1 types which each type throws (0.06 per cent. from the 2n + 3 · 4 type of 2.47 per cent. from the 2n + 19 · 20 type). Primaries and secondaries together throw 0.9 per cent. unrelated 2n + 1 types (1.1 per cent. from primaries and 0.7 per cent. from secondaries). Since diploids threw 13,000 offspring with only 0.16 per cent. 2n + 1 types, it is evident that primary non-disjunction must be more frequent in 2n + 1 types than in diploids. (5) Certain types are more frequent among the new mutations than others, even when figures are corrected for differences in viability. The conclusion is reached that chromosomes differ in their frequency of primary non-disjunction. These differences are not related to chromosome size.

(To be concluded)

SHORTER ARTICLES AND DISCUSSION

ON THE STRUCTURE OF THE HAIR OF THE SEI WHALE (*BALAENOPTERA BOREALIS*)

THE Sei whale, or Rudolphi's rorqual (*Balaenoptera borealis*), one of the mystacocetian or whale-bone whales, of the family *Balaenopteridae*, is a species about fifty feet in length; dark slate grayish or brownish above and white below, with the ventral surfaces of the tail flukes a bluish gray. It is found in the temperate portions of all the oceans of the globe. Recently, through the great kindness of Dr. Ira E. Cornwall, of William Head, Victoria, B. C., the writer received a sample of the hair of this species, consisting of eight shafts. This was a most welcome gift, for among the hairs of mammals already examined in the writer's laboratory, there were none from any member of the *Cetacea*. It was with great interest, therefore, that these were prepared for the microscope and studied.

This preparation consisted in first washing the hairs in a solution of equal parts of ether and 95 per cent. alcohol, followed by a washing in xylol. The shafts were then dried between pieces of filter paper and mounted in paraffin oil, or Euparal (for examination of the medulla, cortex, pigment granules and cortical fusi); or mounted dry (for the examination of the cuticular scales). No special methods were used in the examination of the shafts mounted in a medium, but in the study of the shafts for their cuticular scales they were held in a bit of cork which in turn was held in a "mechanical finger" attachment fixed to the stage of the microscope. In this, as in a capillary rotator, the shafts of the hairs could be turned and the scalation studied on all parts.

The shafts were all extremely stiff and bristly in character; the longest being 23.5 mm; the shortest 14.0 mm; and the average 19.2 mm. In respect of diameters (measured at the middle of each shaft), the maximum was 205.0 μ; the minimum 103.0 μ; and the average, 145.5 μ. In coloration they varied slightly from a pale straw yellowish to white, splotched here and there with irregular patches of brownish gray. These patches were seen under the microscope to consist of agglomerations of amorphous matter, in which were entangled many ovoid tests of

diatoms, from 8 to 20 μ along their major axes (Fig. 1).[1] None of the shafts terminated in a natural end, but were broken off irregularly, and showed evidence of having been much worn and smoothed after the break had occurred. Along the sides of the shafts, likewise, wear had broken off and fractured the cuticular scales, freeing the cortical cells, which had frayed out and gave the shaft a ragged appearance under the microscope (Fig. 2). None of the shafts possessed bulbs, but terminated irregularly, as did the tips.

Of the component elements of the typical mammalian hair shaft (*viz.*, cuticular scales, cortical cells, medulla, pigment bodies and diffuse stain, and cortical fusi) all were present, except, perhaps, the medulla, in characteristic association. The status of each of these will be briefly considered.

The *cuticular scales* were extremely fragmental, and were represented only by vestiges here and there. In all the eight shafts, only a very few perfect scales were found (Fig. 3). Enough of this element of the hair structure was present, however, to make a reconstruction of the scalation possible, and to indicate that the scales were of the *flattened imbricate type* (Fig. 4), similar to those characteristically occurring on mammalian hair-shafts of this diameter. It was a matter of interest to note that these hairs (the first of any from a cetacean to be examined), exhibited the same relationship between cuticular scale-form and shaft-diameter as had been found to be the almost invariable correlation in the hairs of other mammals.[2]

The *cortex* was made up of the usual long, fusiform, somewhat shrunken cells, with their elongate nuclei, characteristic of this element of the hair-shaft structure. The cells were closely amalgamated and fused into a homogeneous, hyaline mass, and showed here and there (under the oil immersion objective) nuclei which differed from the ordinary thin filamentous or broken sort, in that they were slender moniliform structures, somewhat different, in the regularity of their component bead-like masses, from any that the writer had seen in other hairs.

[1] These brought to mind the problematical alga-like bodies found on the hairs of the fossil sloth, *Nothrotherium:* (L. A. Hausman, "The Ovate Bodies of the Hair of Nothrotherium shastense," *Am. Jour. Sci.*, Vol. 18, Oct., 1929, p. 331.)

[2] L. A. Hausman, "Recent Studies of Hair Structure Relationships," *Sci. Mon.*, Vol. 30, March, 1930, p. 258.

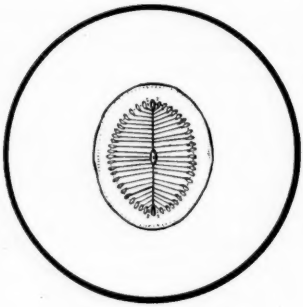

FIG. 1

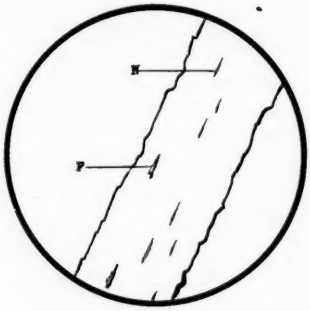

FIG. 2

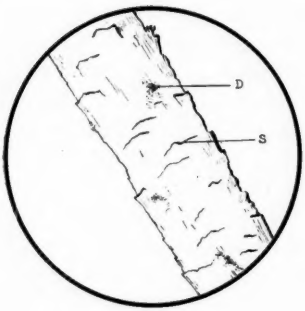

FIG. 3

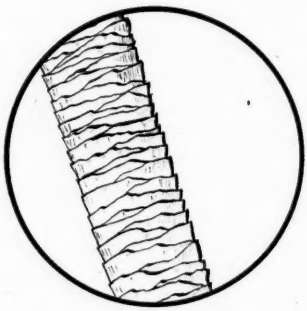

FIG. 4

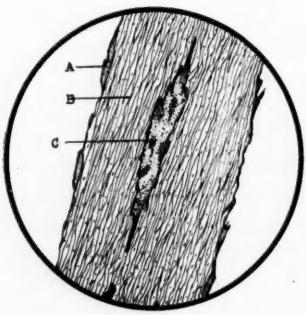

FIG. 5

FIG. 6

LEGEND ON OPPOSITE PAGE

In general, however, the cortex of the hairs presented no new structural features (Fig. 5).

No *medulla* could be found in any of the shafts, and in only one of them any traces of a structure which might possibly have been vestiges of former medullary chambers (Fig. 5). This was a dark, asymmetrical mass of intertwined ropy tissue, thickly enmeshing masses of both fused and discrete pigment granules of a light brown color. In this respect, *viz.*, of the possession of little or no medulla, these hair shafts were similar to those of the same diameter from other species of mammals.[2]

The *pigmentation* of the shafts was both by a diffuse stain in the cortical cells, and by the presence of pigment granules. These were few, and minute (from 1.20 to 0.25 μ along their major axes) and were arranged in those patterns in the cortex of the shaft characteristically associated with hairs of this color (Fig. 6).[3]

The *cortical fusi*,[4] commonly found somewhere in the shafts of most mammalian hairs, were very few. It was difficult, in many instances, to decide whether one were looking at natural fusi, or artificial ones, *i.e.*, *rifts* between the cortical cells caused by strains set up within the hair shafts, from the apparently rough treatment they had received, either while in their place in the skin or after their removal. It was judged that very few natural fusi occurred anywhere within the shafts, except near the bases of the hairs. Fig. 2, N shows the appearance of the natural fusi, and F, of the artificial or fracture fusi.

FIG. 1. Test of diatom occurring on the cuticle of the hair shafts.

FIG. 2. Portion of hair shaft, cleared in xylol, showing irregular outline caused by loss of cuticle and fracturing of cortex, and several fusi. N, natural fusus; F, artificial or fracture fusus.

FIG. 3. Portion of hair shaft mounted dry, showing the vestiges of the cuticular scales. S, scales; D, mass of diatom tests.

FIG. 4. Reconstruction of the flattened imbricate scales of a typical hair shaft midway between its base and tip.

FIG. 5. Optical section through a portion of a shaft midway between its base and tip. A, fragment of a cuticular scale; B, cortical cells; C, vestiges of a medullary mass, with included pigment bodies.

FIG. 6. Cortical pigment granules in patterns as they occur in the cortex.

[3] L. A. Hausman, "Hair Coloration in Animals," *Sci. Mon.*, March, 1921, p. 215.

[4] L. A. Hausman, "The Cortical Fusi of Mammalian Hair," AM. NAT., Vol. 66, Sept.–Oct., 1932, p. 461.

In conclusion, it was found that, in the hairs of the Sei whale, both cuticular scale and medulla structure and form were correlated with the diameter of the hair shafts in the relationships characteristic of mammals in general, and were not, therefore, indicative of the species or of any other taxonomic group.[2] In hair shafts of this general diameter, the presence of the *flattened imbricate* scales, and of little or no medulla (or the *fragmental* type of it) is almost the invariable rule. The pigment granules of the cortex occurred sparsely and in patterns almost always found in hair shafts of this color. The cortical cells and the cortical fusi did not differ essentially from those present in the hair shafts of other mammals.

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A THEORY OF HERMAPHRODITISM

THE fact that sluggish animals are often hermaphroditic has led to the view that sluggishness is the cause of hermaphroditism. Yet many sluggish or attached organisms are not hermaphroditic. For example, among animals the sea snails and other streptoneuran gasteropods are not hermaphroditic; neither are most of the bivalved mollusks. Among plants, the wind-pollinated types are often not hermaphroditic. Numerous other examples of the same sort could be given. Obviously, then, sluggishness in itself does not lead to hermaphroditism.

In very exceptional cases, actively-moving animals are hermaphroditic, as, for example, some of the worms, crustaceans, and one of the fishes (Serranus, of the perch family). But in the vast majority of cases, actively moving animals are not hermaphroditic. This follows from the fact that they move, and therefore tend to scatter. As a result there is a division of labor between the sexes, in so far as the male finds the female and the female produces the young. In many of the backboned animals the males assumed other functions in addition to that of producing sperm and fertilizing the female. Among the herbivores they often came to serve as a bodyguard to the herd. Among the carnivores and in man, they provided the female with food and protection while she was rearing the offspring. In many of the birds the males assisted in the building and guarding of the nest. Thus the separation of the sexes became firmly established among

actively moving animals, even though such animals now often live in groups and no longer tend to scatter.

In attached organisms, however, there is not necessarily any advantage in a separation of the sexes, because attached organisms do not tend to scatter. Therefore the sexes are not necessarily separate in them. Hermaphroditism, on the other hand, may be of advantage to an attached organism. In attempting to find the cause of hermaphroditism, we may consider plants first, as plants are the most common type of attached organism.

Hermaphroditism in plants is connected with the expenditure of the reproductive energy. In general, plants that expend relatively little energy on pollen production are hermaphroditic. Let us see why. Plants that are of equal size expend about the same amount of energy on reproduction. They may, however, expend relatively different amounts of energy on the male and on the female reproductive products. Insect-pollinated species expend relatively less energy on pollen than do wind-pollinated species (which waste a good deal of their pollen in the air). When a species expends comparatively little of its energy on the male reproductive products it can give over most of its reproductive energy to the female products (eggs, embryos, seeds, fruit), and as a rule has come to do so, through natural selection.

There are now several possible ways in which the reproductive "load" can be evenly distributed among the different plants, when a species expends more of its energy on the female than on the male reproductive products. The species may be hermaphroditic, and the female part of each plant may expend more of the reproductive energy than the male part. Or the sexes may be separate, and the females may be more numerous than the males (polygamy), or they may be larger than the males (sexual dimorphism), or they may be longer-lived.

In plants, all but the first of the various possible ways of distributing the reproductive load would be inefficient. For, if there were a great excess of female plants, an insect might visit several of them to the exclusion of the males, and so carry no pollen to them. If the sexes were of unequal size, the larger would shade the smaller; and if the males were shorter-lived than the females, the space left by the dead males would often be occupied by other species.

Hermaphroditism, on the other hand, has no disadvantage for the species. It is therefore the most efficient method of distribut-

ing the reproductive load in plants when the species expends more energy on the female reproductive products than on the male. Therefore all insect-pollinated plants have come, through natural selection, to be hermaphroditic.

Wind-pollinated plants, however, sometimes are hermaphroditic and sometimes they are are not. The reason for this is that many wind-pollinated species expend, apparently, about equal amounts of energy on male and female reproductive products, and in this case there is no particular advantage in hermaphroditism. For, if the sexes are separate, then the reproductive load is equally distributed if half the plants are male, and half female. If the sexes are combined, then the load is equally distributed if half the reproductive energy of each plant is given over to the male reproductive organs, and half to the female. Neither mode of distribution has any advantage over the other. This becomes apparent if it is borne in mind that the sexes mature at different times in a given plant, in species in which the sexes are combined, and at any given time, half the plants of the species are functionally male, half female. Thus, from a functional standpoint it is a matter of indifference whether the sexes are separate or combined, in those species of wind-pollinated plants that expend equal amounts of energy on the male and female reproductive products.

We may now consider animals. For stationary animals, the same rule holds as the one that applies to wind-pollinated plants, as regards the occurrence of hermaphroditism. For, stationary animals can not copulate (since they lack the power of locomotion). They must therefore shed their sperm into the water. But this necessitates the production of the sperm in relatively large quantities, just as is true of the pollen in wind-pollinated species of plants. In case an attached animal expends equal amounts of energy in sperm and egg production, there is no particular advantage to either hermaphroditism or a separation of the sexes, so far as distribution of the reproductive load goes. We therefore find that in attached animals the sexes are either separate or combined. In the sponges, for example, they are combined; in the sea anemones and corals, they are separate.

On the other hand, animals that are not completely attached, but simply sluggish, can transfer their sperm through copulation, and often do, as, for example, snails. Those that do, expend comparatively little energy on sperm production, since they waste none of it in the water or in the process of transfer to some

other animal. They therefore give over a comparatively large amount of their reproductive energy to the female reproductive products. They agree with the insect-pollinated plants in regard to the relative amounts of energy expended on male and female reproductive products. Therefore we would expect them to be hermaphroditic sometimes. But in animals there would often be no particular disadvantage in size differences between male and female, or in other differences between the sexes. Therefore we should expect to find not only hermaphroditism among them, but also polygamy, sexual dimorphism and difference in life span of male and female. These are equally effective ways of distributing the reproductive load, in the case of sluggish animals that copulate, and all of them in fact occur. Which of them a species employs depends probably upon the mode of life of the particular species, though it may often be difficult to see just how. For example, the land snails are hermaphroditic, the sea snails (in some instances at least) polygamous.

Animal parasites are often hermaphroditic, especially those that live in an isolated manner in the internal organs of other animals. For them, hermaphroditism has a special advantage. For sometimes just one parasite might be lodged in an organ. If the sexes were separate, the parasite would die without having offspring. Even if two or more parasites were in the organ, they might all be of the same sex and have no offspring. But if the sexes were combined, the parasites could fertilize themselves. Hermaphroditism is therefore of advantage in isolated parasites, in that it insures fertilization.

But most hermaphrodites are not reproductively isolated. For example, insect-pollinated plants can readily exchange their pollen through the agency of insects. Therefore they are not isolated, from a reproductive standpoint. Neither are sluggish animals, such as snails. They usually live in groups, and are easily accessible to one another. Therefore, the usual cause of hermaphroditism is not reproductive isolation. Its usual cause is to be found in connection with the distribution of the reproductive load. Hermaphroditism represents a very efficient distribution of the reproductive load in organisms that are stationary or sluggish, and that expend less energy on the male than on the female reproductive products. It has therefore come to be the prevalent mode of distribution of the reproductive load in the organisms in question.

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THE PRODUCTION AND INHERITANCE OF EYE DEFECTS IN RABBITS

THE purpose of this communication is to present briefly a comparison of our results with those of Guyer in inducing eye defects in rabbits. After this comparison has been made we shall point out possible reasons for the discrepancies in the two sets of findings. A report on part of our work has already been published,[1] and a statement concerning the remainder is in press.

Guyer used three different methods in inducing eye defects in rabbits. All three had a common purpose, which was the introduction into the pregnant animal of an antibody specific for lens material. By passing from the mother to the fetus, this antibody was to act directly on the eyes of the fetus and cause either a precipitin reaction (milky-looking lenses) or a cytolytic one (destruction of lens material and a resultant effect on the eye as a whole.)

Guyer's three methods, given in the order in which we attempted to duplicate them, were (1) the production of an anti-lens serum in hens by the direct injection of rabbit lenses, and the subsequent introduction of this hen serum into pregnant rabbits, (2) needling the lenses of pregnant rabbits, thereby enabling them to produce the antiserum with their own lenses, and (3) producing the antiserum in the rabbit directly by the injection of lens material.

By the first, or hen-serum method, Guyer obtained offspring from thirteen different treated rabbits. Ten of these produced only normal-eyed offspring, while the remaining three had, besides normal-eyed offspring, seven with badly defective eyes and five with eyes that were slightly abnormal. The total number of young from the thirteen females was sixty-nine.[2] A complete report does not seem to have been given by Guyer on the second, or needling, method.[3] Two out of seven needled females had defective-eyed young. One of these females had a litter of eight, all with chalky-looking lenses, and the other had only two offspring that lived through infancy, both of them, however, having opaque lenses. The total number of young produced by

[1] H. L. Ibsen and L. D. Bushnell, *Jour. Exp. Zool.*, 58: 401–421, 1931.

[2] M. F. Guyer and E. A. Smith, *Jour. Exp. Zool.*, 26: 65–82, 1918; 31: 171–223, 1920; 38: 449–475, 1924.

[3] M. F. Guyer, AMER. NAT., 59: 97–114, 1925.

the seven needled animals was not given. Eleven females reproduced after being subjected to the third, or direct injection method. Only one, however, had any defective-eyed offspring. There were fifty-two normal-eyed and two defective-eyed young.[4]

For the three methods combined Guyer had a total of thirty-one treated females that reproduced, and, of these, six produced some defective-eyed young. The total number of offspring was approximately 150, twenty-four of which had eyes noticeably defective. Thus, one out of every five females had at least one defective-eyed offspring, and about one out of every six of the offspring was defective-eyed.

In our experiments not one of the immediate offspring of treated females had eye defects that were discernible without the aid of optical instruments, and our numbers, with the exception of those obtained by the first method, were considerably larger than those of Guyer. Eleven females that were treated with sensitized hen serum produced fifty-nine offspring. Thirty-one, whose eyes were needled, produced 170, and twenty-six injected with lens material gave birth to 186. Thus, the total number of treated females was sixty-eight, and the total number of offspring, 415.

Although no eye defects appeared in the immediate offspring of our treated females, a few defective-eyed animals were found in later generations. The offspring of the females given sensitized hen serum were not bred and hence there were no descendants. On the other hand, a number of the offspring of the needled animals were mated and the stock was carried on for a few generations. Altogether, 368 animals were produced, five of them having defective eyes. Six individuals with badly defective eyes were also found amongst 920 animals of untreated ancestry. The defective-eyed animals from both groups proved to be related, which led us to the conclusion that heredity, independent of the needling, was the underlying cause for all eleven cases. The mode of inheritance, however, was never determined since sterility and disease put an end to the breeding operations.

Similarly, the offspring of the directly injected (third method) animals were mated, and the breeding continued for several generations. All except three of the 207 animals produced were normal-eyed. The three with defective eyes came from one litter, and constituted the entire litter. There were fairly good indi-

[4] M. F. Guyer and E. A. Smith, *Jour. Exp. Zool.*, 38: 449–475, 1924.

cations that their eyes had become defective through infection by disease-producing organisms. Thus we have proof that there are at least two other causes, besides the one suggested by Guyer, for eye defects in rabbits. We are satisfied, however, that neither of these would account for very many of the defects obtained in his experiments. In the first place, his stock was procured from various sources, and it does not seem reasonable to assume that an hereditary taint would permeate all of it. In the second place, one would not expect disease-producing organisms to attack only the offspring of treated animals.

Since many of our treated animals, especially those receiving direct injections of lens material, gave very high precipitin reactions, one would expect some effect to be produced on the eyes of the fetuses if the antibody passed from the mother through the placenta. So far as we can determine there is no reason why the reaction within the fetus should be radically different from that occurring in a test-tube. With the above considerations in mind, we have come to the conclusion that in our animals little or no antibody passed through the placenta, while in Guyer's the penetration was sufficient to cause eye defects in about one-sixth of the offspring of treated females.

A possible explanation for this difference in placental permeability has been suggested by Guyer.[3] A number of his animals struggled during handling, and he is of the opinion that this may have caused ruptures in the thin membranous walls within the placenta, thereby permitting some of the maternal blood to enter the fetus. We were aware of Guyer's mention of such a possibility at the time we began our experiments, but decided to avoid complications by handling our animals in the conventional manner, which reduces struggling to a minimum. Most rabbit breeders pick up their animals with one hand by the loose skin over the shoulders, and after they have them off the floor of the cage they place the other hand underneath to remove as much strain as possible from the skin that is being grasped. Struggling usually occurs only when the animals are held improperly, as, for example, by the ears alone.

Guyer states that he has no experimental proof for his proposed explanation. It seems to us that his work will never receive full acceptance until the question of the cause, or causes, for placental permeability has been answered. When it becomes possible for others to produce the defective-eyed animals experi-

mentally, the more fundamental phase of Guyer's work—the inheritance of these defects—can then be investigated. As previously stated, we feel that if an appreciable amount of lens antibody passed through the placenta into the fetus some effect should be produced on the eyes of the fetus. The production of such eye defects, however, does not by any means necessarily imply that they will be inherited. It is well known that Guyer maintains, and has furnished evidence, that they are inherited, but a statement of such importance should be amply verified by others before receiving full acceptance. Needless to say, such verification can not be made until the technique of his method for inducing eye defects has been improved sufficiently to insure dependable results.

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INTERLOCKING AS A "DEMONSTRATION" OF THE OCCURRENCE OF CROSSING-OVER

IN a recent issue of the AMERICAN NATURALIST, Mather (1933) has presented a case of chromosome interlocking in Lilium, which he considers as evidence in favor of the partial chiasmatypy theory of chasma formaton and crossing-over. The photographs of these chromosomes are of no value, but Mather's diagram shows a loop of one of the bivalents interlocking with two loops of the other and a single chiasma between the two loops. Such a configuration could arise, on the classical theory of chiasma formation, only if two chiasmata were originally formed between these two loops, followed by a break in one of the chiasmata. Mather recognizes this point, but argues that the reduction in chiasma frequency is so small that such an explanation is invalid. But a break in only one chiasmata would be necessary to explain the figure obtained. Belling (1928) found in Lilium an average of 39 nodes or chiasmata at diplotene, and about 22 at metaphase—a reduction of more than one chiasma per bivalent. Similar observations have been made by the writer. In view of these observations and the fact that Mather's argument is based on a single figure, the proof of the "demonstration" may well be questioned.

More than a thousand interlocking bivalents have been examined in Tradescantia by Edgar Anderson and the writer (1933 and in press). The figures are so clear that photographs of the

preparations are almost diagrammatic in showing the nature of interlocking chromosomes. As a rule, interlocking was found only between ring chromosomes, but in twenty-four cases observed, one of the interlocking bivalents had two loops. In twenty of these figures, interlocking involved the proximal or spindle fiber loop, and in only four figures was the interlocking through the distal loop of the double ring chromosomes. If the partial chiasmatypy theory of chiasma formation is correct, the interlocking, if at random, should involve either the proximal loop or the distal loop with equal frequency.

On the classical theory of chiasma formation, distal interlocking should be comparatively rare. Of all cases of interlocking observed in Tradescantia only 0.6 per cent. were distal, and among the cases involving one bivalent with two loops, only 17 per cent. were distal. The evidence supports the classical theory of chiasma formation, but it can not be considered as a critical "demonstration," because the type of initial interlocking at pachytene is not known, and it may not be at random for all loci.

Although Janssen's partial chiasmatypy theory has received considerable support in recent years, little critical evidence has been produced. Belling's (1923) explanation of the mechanism of crossing-over is logical in many respects, but it is based on detailed studies of connecting fibers, so near the limits of visibility that the evidence is by no means conclusive. The "demonstrations" of the mechanism of crossing-over, so far presented by Mather, Darlington, *et al.*, are valid only if the unproved assumptions regarding chiasma formation are correct.

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